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OCCUPATIONAL PRESSURE NEURITIS OF THE DEEP PALMAR BRANCH OF THE ULNAR NERVE

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FOCAL atrophic paralysis of the small muscles of the hand without cutaneous sensory disturbances may be caused by the benign disorder of neuritis of the deep palmar branch of the ulnar nerve as well as the syndromes of amyotrophic lateral sclerosis and myelopathic muscular atrophy (Duchenne-Aran disease). It is of clinical importance to differentiate these disorders. Neuritis of the deep palmar branch of the ulnar nerve is rarely reported in the literature, although it may not be of rare occurrence. For this reason the following patient is presented.

REPORT OF A CASE

A. T., a 50 year old white married telephone cable splicer, was admitted to the hospital Nov. 20, 1947, with a chief complaint of "loss of strength in the right grip." The patient, in robust good health, noted the sudden painless loss of strength in his right hand while at work six weeks prior to admission. There were no paresthesias, numbness, coldness, sweating or systemic symptoms. The patient was at work performing the labor he had done regularly for thirty-one years. This consisted in using a pair of small wire-cutting shears many hundreds of times each day in such a manner that a horny callus was formed on the inner side of the hypothenar eminence 4 cm. proximal to the fourth metacarpophalangeal joint. He did not rest his elbows on any support and had never suffered an injury to his forearm or ulnar nerve. There was no evidence of nutritional deficiency, alcoholism or exposure to toxic chemicals. Since the onset of the weakness the patient has been unable to perform his work. There was also some clumsiness in writing, shaving and handling table utensils, and he noticed buckling and weakness when firmly pressing the extended finger tips of the right hand against a resisting surface. During the six weeks prior to admission, there had been no improvement in strength and atrophy of the space between the thumb and index finger was noted.

Conditions revealed on the physical and neurologic examinations were within normal limits except for the right hand. The callus was seen on the palm of the right hand as described. It was adherent to deeper structures as demonstrated by a dimpling when the fingers were extended. The little finger was per-

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manently in an abducted position because of loss of function of the fourth palmar interosseus muscle together with the unopposed action of the extensor digiti quinti and a portion of the extensor digitorum (according to the analysis by Wartenburg),[1] as well as the abductor minimi digiti, which was normal in this patient. There was guttering wasting of the interosseus muscles and moderate wasting of the space occupied by the adductor pollicis between the thumb and index finger. Fanning of the fingers and bringing them together were done weakly, and the little finger could not be adducted at all. There was noticeable weakness on attempts to grasp a piece of paper between the thumb and index finger held in extension, demonstrating the paralysis of the adductor pollicis muscle (Froment's *signe de journal).* By contrast, the strength of opposition of the thumb and little finger, the power of abduction and flexion of the little finger, and all movements at the wrist were normal. Thus motor testing revealed that whereas the dorsal and volar interosseus, fourth and third lumbrical and adductor pollicis muscles were severely or totally paralyzed, the palmaris brevis, abductor minimi digiti, flexor minimi digiti and opponens minimi digiti muscles were of normal strength.

The exact position of a lesion which would explain these findings is based on the anatomic demonstration that the muscles of the hypothenar eminence are all innervated prior to the interosseus and adductor pollicis muscles.[2] Thus the site of interruption of function of the deep palmar nerve in this patient coincided anatomically with the palmar callus. This fact suggests that the callus contributed the direct compression of the nerve which caused the neuritis.

It was also observed that pressure on the patient's palmar callus produced focal aching pain. Point tenderness is of localizing value in other peripheral nerve pressure injuries as first described by Browning in 1887 and described again in 1901.[3]

Careful testing with cotton, pinpoint and hot and cold stimuli revealed no cutaneous sensory defect. However, an effort to evaluate loss of sensation in deeper structures was made by injecting 5 per cent sterile saline solution into several muscles of the hands. Whereas only 0.1 cc. of solution would cause severe aching pain on injection into the normal left adductor pollicis muscle, five times as much solution caused no discomfort on injection into the paralyzed right adductor pollicis. This observation was repeated by both volar and dorsal approaches to the muscle. Injection of only 0.1 cc. into the abductor minimi digiti muscle of either hand caused severe aching pain. Thus the sensibility of the muscle to a noxious stimulus was absent in the paralyzed muscle and normal in muscles with normal motor function. It was concluded that the deep palmar branch of the ulnar nerve is not exclusively motor

1. Wartenburg, R.: A Sign of Ulnar Palsy, J. A. M. A. **112**:1688 (April 29) 1939.

2. Sunderland, S., and Hughes, E. S. R.: Metrical and Non-Metrical Features of the Muscular Branches of the Ulnar Nerve, J. Comp. Neurol. **85**:113, 1946.

3. Browning, W.: The Tender Point in Pressure Paralysis of Peripheral Nerves, Kansas City M. Index Lancet **22**:6, 1901.

but that it contains the sensory fibers to the muscles which it supplies, although it may conduct no cutaneous sensation. The point tenderness at the site of callus compression is additional evidence that the nerve carries afferent impulses.

RÉSUMÉ OF THE LITERATURE AND COMMENT

Atrophic paralysis of the muscles supplied by the deep palmar branch of the ulnar nerve was first described by Hermann Gessler in 1896 [4] under the title of "A Peculiar Form of Progressive Muscular Atrophy in Gold Polishers." He did not recognize the condition as a neuritis. The first correct formulation was made by Ramsay Hunt in a description of 3 patients in 1908.[5] He subsequently reported on a total of 6 patients in 1911 [6] and 1914.[7] In reviewing the subject in 1930, he added, "Since then I have encountered the condition in both private and hospital practice and I do not consider it a great rarity." [8] Wilfred Harris reported on 2 patients in 1929 [9] and, on finding no previous reports in the literature, commented, "My two cases were first seen in one week so the apparent rarity may be due to want of recognition." Shortly thereafter, in a published letter, C. Worster-Drought [10] reported 4 cases of this disorder. The onset of the paralysis was sudden in each patient, and "in all four cases abduction and opposition of the thumb and little finger were unaffected. As with Dr. Harris I was unable to find adequate description of the condition in the literature." Russell and Whitty [11] recently reported 5 cases and emphasized that the condition "is relatively common" and "apt to be overlooked by the clinician." They pointed out that "the connexion between trauma to the palm of the hand and the onset of the paralysis was quite definite, but it must be emphasized that careful inquiry is often needed to elicit the cause of the injury as the patient is usually unaware that he has

4. Gessler, H.: Eine egenartige Form von progressiver Muskelatrophie bei Goldpolirinnen, Med. Cor.-Bl. d. wurttemb. ärztl. **36**:281, 1896.

5. Hunt, J. R.: Occupational Neuritis of the Deep Palmar Branch of the Ulnar Nerve, J. Nerv. & Ment. Dis. **35**:676, 1908.

6. Hunt, J. R.: The Thenar and Hypothenar Types of Neural Atrophy of the Hand, Am. J. M. Sc. **141**:224, 1911.

7. Hunt, J. R.: Neural Atrophy of the Muscles of the Hand Without Sensory Disturbances, Rev. Neurol. & Psychiat. **12**:137, 1914.

8. Hunt, J. R.: Thenar and Hypothenar Types of Neural Atrophy of the Hand, Brit. M. J. **2**:642, 1930.

9. Harris, W.: Occupational Pressure Neuritis of the Deep Palmar Branch of the Ulnar Nerve, Brit. M. J. **1**:98, 1929.

10. Worster-Drought, C.: Pressure Neuritis of the Deep Palmar Branch of the Ulnar Nerve, Brit. M. J. **1**:247, 1929.

11. Russell, W. R., and Whitty, C. W.: Traumatic Neuritis of the Deep Palmar Branch of the Ulnar Nerve, Lancet **1**:828 (June 14) 1947.

damaged his hand in any way." These authors also made the general statement that "there is no sensory loss," which should be amended in the light of tests of muscle sensation as described in this report.

Attention is called to the similarity of this disorder to the syndrome described by Wartenburg in 1939 [12] of a focal atrophy of the thenar eminence without any change in sensation (cutaneous ?). It was postulated that this disorder was caused by an occupational pressure neuritis of the thenar branch of the median nerve, as first described by Ramsay Hunt in 1909.[13]

There is a striking similarity between the case reported in this paper and the one described by Drooz in 1947 [14] under the title of "Benign Focal Amyotrophy." His patient had a localized atrophy of the small muscle between the thumb and index finger which had appeared over a period of several weeks and caused him difficulty in handling table silver. The published photographs of the hand of this patient closely resemble those of the hands of patients with neuritis of the deep palmar branch of the ulnar nerve. Drooz emphasized the absence of sensory signs and symptoms (although only cutaneous sensitivity is reported on). He rejected the diagnosis of neuritis because the atrophy was limited to the adductor pollicis muscle and was unassociated with the electrical reaction of degeneration. However, as Drooz pointed out, this is not an incontrovertible argument against a neuritic origin. There was no such reaction of degeneration in our patient, A. T. Since the adductor pollicis is the last muscle to be supplied by the ulnar nerve, it is the one muscle that could be paralyzed in isolation by a peripheral neuritis of the ulnar nerve. Drooz's assumption that his patient had a special type of amyotrophy could be more firmly established if he had found that the injection of hypertonic saline solution into the atrophied adductor muscle caused severe aching pain. However, if this muscle were insensitive to noxious stimulation, neuritis would have to be considered.

Another condition which may be confused with neuritis of the deep palmar branch of the ulnar nerve is "tardy paralysis of the ulnar nerve," which may come on years after an injury to the ulnar nerve at the elbow. This disorder, named by Ramsay Hunt in 1916,[15] can be ruled

12. Wartenburg, R.: Partial Thenar Atrophy, Arch. Neurol. & Psychiat. **42**:373 (Sept.) 1939.

13. Hunt, J. R.: Neuritis of the Thenar Branch of the Median Nerve: A Well-Defined Type of Atrophy of the Hand, Tr. Am. Neurol. A. **35**:184, 1909.

14. Drooz, R. B.: Benign Focal Amyotrophy, Arch. Neurol. & Psychiat. **58**:498 (Oct.) 1947.

15. Sheldon, W. D.: Tardy Paralysis of the Ulnar Nerve, M. Clin. North America **5**:499, 1921. Hunt, J. R.: Tardy or Late Paralysis of the Ulnar Nerve, J. A. M. A. **66**:10 (Jan. 1) 1916.

out by careful history of possible injury, by the absence of valgus deformity at the elbow and by the absence of changes in cutaneous sensation.

Also to be noted is traumatic severance of the deep palmar branch of the ulnar nerve, which may produce the expected picture with the prominent absence of any alteration in cutaneous sensation. Penetration of the palm by a nail, knife or other object is, of course, obvious.

Neuritis of the deep palmar branch of the ulnar nerve is stated by the previously mentioned authors and by Wilson [16] to be due to injury from continued and repeated compression of the nerve by the handle of some tool or in some other local way, such as gripping the handlebar of a motorcycle too firmly. The workmen most liable to this neuritis include gold and brass polishers, cobblers who use the leather-cutting knife, jewelers who file metals, machinists and motorcyclists. In all the reported cases the patients have had unilateral involvement. Hunt attributed the damage to a pinching of the nerve as it passes between the small muscles of the hypothenar eminence near their origins. Harris postulated a compression of the nerve against the heads of the metacarpal bones. Anatomic dissection in support of either theory has not been offered.

SUMMARY AND CONCLUSION

The case of a patient with occupational pressure neuritis of the deep palmar branch of the ulnar nerve is presented. The neuritis was associated with a callus which overlay the postulated site of nerve injury. This site was distal to the innervation of the hypothenar muscles, which were spared, but proximal to the remaining interosseus and adductor pollicis muscles, which were paralyzed and atrophic. There was no loss of cutaneous sensation. All previous reports have emphasized this absence of sensory disturbance but have failed to observe that this is limited to cutaneous sensitivity. Muscle sensitivity to noxious stimuli was demonstrated to be impaired in this subject. Thus no pain was induced by the injection of hypertonic saline solution into the atrophic adductor pollicis muscles.

It is suggested that this simple procedure can be used to distinguish between a neuritis, on the one hand, and either myopathy or progressive spinal muscular atrophy, on the other hand, as a cause of atrophic paralysis associated with normal cutaneous sensation.

16. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940, vol. 1, p. 333.

ASYMBOLIA FOR PAIN

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CLINICAL neurologists have observed patients who do not react to painful stimuli and yet have no anesthesia. Some of these patients, instead of withdrawing, will sometimes actually proffer their limbs for the pinprick. In such a case an inexperienced examiner when carrying out a routine sensory examination might note that pain sensation was normal, inasmuch as the patient could distinguish between sharp and dull equally throughout the body. Or, on the contrary, he might report that there was generalized hypesthesia when the patient stated that the pinprick did not hurt.

Asymbolia for pain denotes the inability to recognize the unpleasant or disagreeable component of a painful or threatening stimulus, with the result that little or no defense reaction is produced, although the noxious stimulus itself is perceived. Although related to apraxia, it is characterized by the fact that it is a type of apraxia only in this distinctive sphere of reaction to pain and danger. Schilder noted that the apraxia usually became evident only in actions directed against the patient's own body. He then added: "It is not alone the expression of a deficiency. There is also a particular attitude toward pain which lacks the integration into a higher propositional act."

Pain asymbolia must be distinguished from other conditions which bear a superficial resemblance to it, such as generalized analgesia due to lesions in the nervous system, hysterical anesthesia and congenital insensitivity.[1] Another type of decreased or absent reaction to pain which may be psychologically related but which is clinically distinct from pain asymbolia is that found in psychotic persons, particularly those with catatonic schizophrenia. These patients often hurt or mutilate themselves without showing the slightest apparent sign of

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1. Kunkle, E. C., and Chapman, W. P.: Insensitivity to Pain in Man, A. Research Nerv. & Ment. Dis., Proc. **23**:100, 1943. Ford, F., and Wilkins, L.: Congenital Universal Insensitiveness to Pain, Bull. Johns Hopkins Hosp. **62**:448, 1938. Dearborn, G.: A Case of Congenital General Anesthesia, J. Nerv. & Ment. Dis. **75**:612, 1932.

pain. Bender and Schilder [2] divided these reactions into two types, according to the dominant mental symptoms of patients they studied. Those with stupor but without marked tension showed no reaction whatsoever to pinching, pinprick or blows but rapidly and vigorously withdrew on faradic stimulation. Patients with pronounced "tensions" frequently reacted to prolonged application of painful stimuli—i. e., pinching or electric shock—but in an inadequate and local way. For instance, there might be squirming or athetoid movements of the fingers, sometimes spreading up to the arm, occasionally accompanied with change in respiratory rate, with tears in the eyes or with stiffening of the body. The response is rather a postural attitude than an action of escape or defense. One of our patients, a man with catatonia, would roll his head from side to side whenever he was painfully stimulated but never withdrew his limbs. This perverted reaction disappeared when his catatonic state cleared up.

Schilder and Stengel [3] in 1928 called attention to this phenomenon, which they designated, in a patient showing organic disease of the brain, asymbolia for pain. They further elaborated on this condition in 1931 and reported 10 cases, with anatomic localization of the lesion either at autopsy or at operation in 3. The predominant lesion was in the supramarginal gyrus, with some involvement of the gyrus angularis and superior temporal gyrus in the dominant hemisphere. Six of the patients had a perceptive aphasia. The etiologic factors varied among vascular disease, tumor, syphilis and head injury.

Since the original descriptions of the clinical syndrome by Schilder and Stengel there have been no reports of such cases. Recently we have found several instances of pain asymbolia, and we therefore thought it worth while to report four of the cases.

REPORT OF CASES

CASE 1.—E. C., a 70 year old former Sunday school teacher, was admitted to Bellevue Psychiatric Hospital on Aug. 1, 1946 because of incoherence in her speech. There were no illnesses in her past history except peripheral facial palsy in 1932. In June 1945 her physician had noted that she had a mild right hemiparesis. At that time her blood pressure readings were 230 systolic and 140 diastolic. Within three months the right-sided paresis disappeared except for residual weakness and stiffness of the hand, but it was noted that she was unable

2. Bender, L., and Schilder, P.: Unconditioned and Conditioned Reactions to Pain in Schizophrenia, Am. J. Psychiat. **10**:365, 1930.

3. (*a*) Schilder, P.: Cortical bedingte Steigerung von Schmerzreaktionen, Ztschr. f. d. ges. Neurol. u. Psychiat. **132**:367, 1931. (*b*) Schilder, P., and Stengel, E.: Schmerzasymbolie, ibid. **113**:143, 1928; (*c*) Der Hirnbefund bei Schmerzasymbolie, Klin. Wchnschr. **12**:535, 1928; (*d*) Das Krankheitsbild der Schmerzasymbolie, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:250, 1930. (*e*) Schilder, P.: Notes on the Psychopathology of Pain in Neuroses and Psychoses, Psychoanalyt. Rev. **18**:1, 1931.

to recall names or correctly remember faces. In June 1946 she had another stroke, and on July 7 her physician again found weakness of the right side of her body. Her speech was good, and she was mentally normal except for some irritability. On July 15, he noted beginning incoherence of speech. This apparently was an aphasia, which became progressively worse. She had difficulty in recognizing people, was careless of her appearance and in her habits and showed some paranoid delusions.

On admission the general physical examination showed generalized arteriosclerosis, systolic murmur at the apex with extrasystoles and blood pressure reading of 180 systolic and 90 diastolic.

Psychiatric Status.—The patient showed complete awareness of, and interest in, her surroundings. Her speech was usually rapid, with tendency toward perseveration and repetition of words. Some words were often unfinished, and she frequently had difficulty in finding the correct one. The perseveration was present also in the motor sphere and was manifested by repeated gesticulations, often accompanied with marked emotional outbursts without provocation or apparent motivation. Otherwise there was an apparently normal affect. Memory for recent and remote past events was impaired. Orientation was also poor. Her responses were relevant, but subsequent associations were frequently irrelevant. There were no hallucinations. She expressed vague delusions to the effect that her family threatened to take away whatever savings she had.

The patient was observed for several months in the neurologic service. An outstanding feature of her performance on testing was the definite day to day fluctuation of her symptoms and capabilities. Sometimes she showed an excellent score; at other times, a very poor one.

Neurologic Examination.—Neurologic examination revealed a residual left-sided facial palsy with synkinesias and contracture. The ocular fundi showed arteriosclerotic changes. Perimetry was not possible, but gross testing revealed an apparent defect in the right homonymous half fields of vision with double simultaneous stimulation. There was a slight tremor bilaterally on the finger to nose test, more pronounced on the right.

On the first examination for pinprick sensation, it seemed as if the patient had a generalized analgesia. She gave this impression even when she was told that "this is going to hurt you." She then answered "didn't hurt me" when the examiner pricked her to the point of drawing blood. Subsequently, response to pain was tested daily with pinprick. On rare occasions there was a partial and ineffectual withdrawal action, usually when the stimulus was applied without warning. Otherwise the patient continued to show complete lack of withdrawal to painful stimuli (pinprick). General sensation was otherwise relatively intact. She could distinguish between sharp and dull throughout on repeated or maintained pinprick. Light touch (scratching) was likewise perceived. Point localization was good for tactile and thermal stimuli. She could recognize varying degrees of hot and cold throughout, but she would place her hands in uncomfortably hot or ice water and make no attempt to withdraw them, merely identifying it as hot or cold. When a lighted match was placed in her hands, she held it until her fingers were burned, instead of dropping it or blowing it out. The integrity of position and vibration sense was difficult to evaluate because of inattention, but after repeated tests it was felt that there was relatively little impairment, if any. There was dysstereognosis bilaterally. Sometimes the patient was

able to indicate her recognition of the test object by showing how to use it, although she was unable to name it because of her anomia. Texture and smoothness could not be recognized.

The extinction phenomenon was present in about 75 per cent of repeated trials; the patient selected her left side on bilateral simultaneous stimulation by pinprick, heat or cold.

Autonomic Reactions to Pain.—Rapid painful stimuli (pinprick) provoked no noticeable changes, but prolonged pinprick produced pupillary dilatation and a rise in blood pressure (20 mm. systolic and 10 mm. diastolic), even when no defense reaction was manifest. A test of muscle ischemia was performed by inflating a blood pressure cuff on the arm to the point of completely occluding the vessels. The patient was able to clench her fists rapidly 34 times. She apparently stopped because of fatigue rather than pain (the examiner who accompanied her was also extremely fatigued). After intravenous injection of 1 cc. of histamine phosphate solution (1 : 1,000) sweating and flushing of the face occurred and she complained of warmth but did not complain spontaneously of headache, although she grimaced somewhat. When questioned, she admitted having some slight pain in the frontal region, which did not persist for more than a few minutes.

In addition to the lack of reaction to painful body stimulation, when the examiner threatened her with an aggressive gesture, such as slapping her face, punching her nose, pinching her or even moving a pin toward her eyes, she did not flinch, blink or react emotionally. However, if told that she would be slapped or struck without any accompanying gesture, she would respond vigorously, saying, "Don't you slap me, or I'll slap you right back," or "Don't you dare punch me," understanding the unpleasant significance of the act.

Visual tests showed visual extinction to be always present; with simultaneous finger movements in her peripheral visual fields on both sides of her head, the left was always indicated first; she indicated the right hand only on continued movement after removal of the left hand. When she was confronted with a series of commonplace articles, two of each kind scattered over the table, she almost always selected the article named by the examiner from the left side of her field, ignoring the one on the right. The same preference was noted in the wool sorting test and in selection of letters from a jumbled alphabet card.

Agraphia was present, although the patient had no insight into her inability to write and maintained that she was well able to do it. She could occasionally reproduce a correct letter of her name but generally wrote a nondescript scrawl, going off the edge of the paper. Simple geometric figures could sometimes be copied well but very poorly at other times. There was difficulty in copying Bender's gestalt figures.[4]

Spatial localization for auditory stimuli was good, the source being correctly pointed out from either side, laterally, above or below her.

Aphasic Symptoms.—There was an anomia for habitually used objects (key, fountain pen, flashlight, etc.), although after handling the object for a short time the patient would usually name it spontaneously. She had no asymbolia for use of objects. When several articles were named, she pointed them out. Orders were understood and carried out quickly. Alexia was present for single words and sentences; individual letters were sometimes recognized, sometimes not, in which case the letters "G," "H" and "I" were most frequently used. The word "cat"

4. These are a series of compound irregular geometric designs as embodied in Lauretta Bender's tests for organic disease of the brain.

was spelled "cig" or "cit," but when shown the written word she would correctly pronounce "cat" after several attempts. A watch was always correctly read and the time correctly stated. When she was shown a picture of several persons, she at first said, "This is an H, a G," and then a moment later spontaneously corrected herself by describing the persons correctly. When many drawn geometric figures in a small field (circle, square, cross, dot, triangle) were placed before her, she could not spontaneously name them, but when she was given the name by the examiner she picked out the correct object in about 75 per cent of her trials, without preference for either side of the field. There was no apraxia for simple acts, such as opening a pin with either hand, using a pen or lighting a match. But a definite constructional apraxia was evidenced by her performance on the Kohs Block Test, when she was unable to reproduce even the simplest design. Similarly, she was unable to reconstruct a square of matchsticks after having been previously shown how.

Body Schema.—Simple movements involving the use of her body were well carried out. She pointed out parts of her body rapidly, and usually correctly, except that she showed a constant agnosia in both naming and identifying named fingers. However, complex orders requiring simultaneous recognition of several parts of the body could not be carried out. She showed no right-left disorientation on her own body but frequent confusion in identifying the examiner's right-left, indicating a visual spatial disorientation. This was also shown by her inability to reproduce complex hand postures involving visuopostural correlations, although she could imitate simple gestures.

Although she was able to count to 20 fairly well, she could not reverse herself and otherwise had acalculia.

Laboratory Data.—Roentgenograms of the skull showed no abnormalities. An electroencephalogram showed some low voltage fast activity in the motor regions bilaterally. Activity in the right postparietal region was slightly more rapid than in the corresponding areas on the left. A pneumoencephalogram showed anterior horns of the lateral ventricles to be symmetric as to size, shape and position; the posterior horns were dilated and asymmetric, the left being larger than the right. There was considerable air in the great cerebral fissure, and there were slightly dilated sulci in the temporoparietal regions, interpreted as indicating cortical and subcortical atrophy in the temporoparietal regions, more pronounced on the left.

Case 2.—B. G., a 53 year old well nourished white man, right handed, was admitted to the Neurological Service of the Mount Sinai Hospital because of dizziness, headache and disturbance of speech.

In 1941 he had occlusion of a coronary artery, with complete recovery. The present episode began five weeks before admission, with sudden onset of dizziness, nausea and pallor, followed by pain in the left frontoparietal region with scintillating scotomas. A week later, he noticed forgetfulness for names of objects and people, difficulty in finding words to speak or write and loss of comprehension of abstract ideas. He seemed unable to understand words. His gait showed a slight leaning toward the left and awkwardness in turning or performing simple acts, such as striking a match.

On admission, a routine systemic examination revealed essentially normal conditions. Neurologic examination revealed unequal pupils, the right being slightly larger than the left, and both reacted well to light and in accommodation. A right homonymous hemianopsia was present. Fundoscopic examination showed arteriovenous nicking, with areas of old hemorrhage and grayish exudate. The temporal border of the left disk was blurred, but no elevation of the nerve head

could be measured. There was a questionable right facial paresis, upper motor neuron type. Deep tendon reflexes were hyperactive throughout, slightly more so on the right, but no pathologic reflexes were elicited. Sensation was normal for all modalities. Motor power was slightly diminished in the right extremities. A slight ataxia and terminal tremor on finger to nose tests was present bilaterally, especially on the right.

Aphasic Phenomena.—There was a mixed aphasia. There was anomia even for familiar objects, both on spontaneous naming or on choice of named objects. This was also manifested in his reading (dyslexia). The patient was able to follow simple commands but not the more complex, involving simultaneous use of several parts of his body. Body parts such as eye, nose, ear and abdomen were localized correctly. However, he made frequent errors when his fingers were tested. This finger agnosia was most constant, not only when he was asked to name them spontaneously but also when he was asked to indicate named ones, even after they were once pointed out. Ideational apraxia was shown in complex actions; for instance, when asked to light a cigaret, he would break it in half instead. Similarly, on the Kohs Block Test, although he could reproduce the simpler block designs after some delay, he could not construct the more complicated ones. The results of this test were interpreted to indicate an inability to learn from experience, an impairment of spatial orientation or relation of figure to background and a tendency to favor a concrete mode of thinking, with difficulty in abstraction. This spatial disorientation was evidenced by confusion in designation of right-left, not only in space but on his own body. He also showed acalculia. Agraphia was present, except that he was able to write a recognizable semblance of his name.

Over a period of about two weeks, there was a progressive aggravation of all symptoms. The aphasia became more marked; predominantly motor on admission, it became equally severe in the sensory sphere. Ten days after admission, it was thought that the patient was apparently less sensitive to pain throughout the right side of his body. The following day, he showed a typical pain asymbolia over his entire body. He would not withdraw his hands or other parts of the body on painful stimulation (pinprick), although he could distinguish sharp from dull. He would even advance his arms for the painful pinprick. Neither was there any response to threatening gestures, such as retreat of his head or blinking gestures of defense.

Laboratory Data.—Roentgenograms of the skull revealed normal conditions except for some calcifications of the falx. An electroencephalogram taken shortly after admission showed a severe depression of alpha activity in the left parieto-occipital region, with absence of delta activity. This was thought to indicate a focal lesion, possibly vascular or neoplastic in nature. Spinal tap yielded fluid that showed a questionably positive Pandy reaction and contained moderately increased protein (58 mg. per hundred cubic centimeters).

Operation.—Craniotomy of the left frontoparietal region revealed greatly increased intracranial pressure as evidenced by the bulging dura and the flattened pale gyri. A gliomatous tumor was found in the inferior parietal lobule. It was excised to a depth of about 2 cm. in the subcortical region, including part of the overlying cortex. Subsequent pathologic study showed the tumor to be a probable transitional glioma.

Postoperative Course.—After operation, there was gradual improvement. The right hemiparesis became less severe and two weeks later was not noticeable

except for a slight residual weakness of the facial muscles. The hemianopsia cleared up progressively, and one month postoperatively only a slight defect was demonstrable in the right peripheral field. However, the right-left disorientation and the finger agnosia remained, although the patient was able to recognize other parts of his body; the mixed aphasia improved slightly. On the contrary, the pain asymbolia disappeared completely within two weeks after operation. At this time he again withdrew in defense against painful stimulation and against menacing gestures. Other sensory tests elicited completely normal reactions.

CASE 3.—J. V., a 19 year old, right-handed youth, was admitted to the hospital on Nov. 12, 1946, with a gunshot wound of the head. On admission, he was unconscious, his left pupil was decidedly dilated and his neck, trunk and extremities were rigid. Deep reflexes were slightly more active on the right, with a Babinski sign present on that side. There was a round wound of entry in the left temporal region and one of exit in the left parieto-occipital region.

Shortly after admission, the patient was operated on. He was found to have a gutter wound of the cortex extending from the point of entrance to the point of exit. The core of damaged tissue measured about 2 inches (5 cm.) in diameter and was filled with blood clot, bone and metal fragments and liquefied brain. The area of cortex removed involved the posterior part of the superior temporal gyrus and parts of the angular and most of the supramarginal gyri.

Recovery from the operative procedure was uneventful. Four days postoperatively the patient had paralysis of the right leg and paresis of the right arm. He showed a mixed aphasia, predominantly emissive. Two days later, on November 20, the right hemiplegia had disappeared except for a slight weakness of the facial muscles. There was astereognosis in the right hand. The aphasia was practically unchanged.

By Nov. 25, 1946, before discharge the patient's speech was returning. He could say a few simple words and count to 10. He seemed to be able to understand most things that were said to him. Sensory examination showed normal perception of pain and touch. The extinction phenomenon was present, though not consistently, on painful stimulation over the hands. There was some withdrawal to pinprick, but this reaction was slow and inadequate.

The patient was readmitted for mental observation on Jan. 1, 1947; it was noted that he was inactive and seclusive. He was dull and retarded, without much emotional reaction. His orientation was good for time and place. His memory was likewise good for both recent and remote events, except for a lacunar amnesia for the shooting and drinking episode which accompanied it. He could not retain or recall three digits. Calculation was fairly good for simple sums but impaired for more difficult ones.

He showed a mixed aphasia and spoke mostly in monosyllables. The expressive component was only slightly impaired as compared with the more noticeable perceptive aphasia. However, most of the time he appeared to understand questions and carried out orders. In addition, there was an anomia for objects which were not of everyday use. Thus his replies were sometimes disconnected or fragmentary, or he perseverated because of his inability to find the correct words. He had no difficulty in reading.

He was able to write his name, but almost nothing else (agraphia). While no agnosia was present for parts of his body, including his fingers, he had some right-left disorientation with regard to his own body. This was particularly evident when he attempted to carry out orders involving several parts of the body or several concepts. There was definite difficulty in identifying right and

left on the examiner and in reproducing postures of the hands in space. Except for this visuospatial postural difficulty he did not show apraxia for usually tested acts—opening a pin or fountain pen, lighting a match, imitating simple positions and hand movements. However, a definite constructional apraxia was found on the Kohs Block Tests; the simplest designs could be reproduced without much delay, but with the more complex patterns he showed perplexity and errors.

The inadequate reaction to painful stimulus noted on his previous admission was now more pronounced and very striking. He would not withdraw his limbs on single stimulation and would withdraw them only slightly after repeated and prolonged pinprick. When stimulated on his face, he would grimace, but he pulled his head backward only after strong, prolonged or repeated pinprick. Complete lack of withdrawal was shown to threatening gestures, although he understood verbal menaces and would protest harmful intention. The degree of reaction varied from day to day when he was repeatedly tested under similar environmental conditions. He was not aware of his lack of reaction, which was still present on his discharge several weeks after admission.

Case 4.—J. McD., a 53 year old woman, was admitted because of memory defects of about six months' duration, and an acute episode of confusion and disorientation of one day's duration.

Her past history was essentially normal except for failing vision for about fifteen years, more advanced in the right eye. For about three years prior to admission she complained of transient episodes of dizziness, usually lasting from a few minutes to several hours. For about six months she complained of forgetfulness, especially for recent events.

Two days before admission she was apparently in her normal condition. The following day she was found sitting in her room, which was in disorder, unable to walk and to answer the door, although she recognized voices and was able to move her limbs. She spoke in an incoherent manner and appeared confused and disoriented.

Systemic examination on admission revealed essentially normal conditions except for a cataract in the right eye and hypertension (blood pressure 200 systolic and 100 diastolic). Neurologic examination revealed that her vision was extremely poor. She could perceive light and moving fingers but could not distinguish forms. There were pronounced arteriosclerotic changes in the retina. The right arm and hand were slightly weaker than the left. Deep tendon reflexes were hyperactive but equal, and no pathologic reflexes were elicited.

The same periodic fluctuation was noted in the severity of her symptoms and in her state of contact as was noted in our other patients.

Although the sensory status was frequenly difficult to evaluate because of the patient's lack of contact, repeated examinations over a long period showed some consistent findings. Light touch and scratching were perceived only over the face on some examinations; on others she felt touch throughout. Hot and cold were consistently distinguished; warm and cool could not be well identified, errors being made in about 50 per cent of the trials. On pinprick, she was able to distinguish between sharp and dull throughout. When severely pricked to the point of drawing blood, she would say "ouch" and occasionally grimace but she never withdrew her limbs or turned her head away. The extinction phenomenon was present almost constantly on her forehead, where she would indicate the right side on simultaneous bilateral touch or pinprick. On her arms, this phenomenon was present in only about 50 per cent of the tests. It was never noted on thermic stimulation.

Aphasic Symptoms.—The patient showed a mixed aphasia, predominantly perceptive. Sometimes she answered questions and obeyed simple orders without hesitation. At other times she would not appear to understand, would answer irrelevantly and would have difficulty in finding words, even speaking a word salad. Visual gnosis could not be tested, but objects manipulated with both hands were correctly named (key, pen, cup, light, fingers, etc.). But when the same objects were placed in either hand, she showed astereognosis, most marked on the right. She was able to spell simple words such as "cat" or "dog" but was unable to reverse them ("cat" backward was "kat"). Acalculia was present for the simplest calculations, although she was able to count from 1 to 10 and then backward after some hesitation. Right-left disorientation on her own body was fairly constant. She was occasionally able to name parts of her body when touched and designate some named parts (nose, tongue, eye) but could not indicate the majority of her other body parts; she manifested a constant finger agnosia. Voices could be accurately localized to either side. Autonomic reactions to painful stimuli were manifested by pupillary dilatation, acceleration of pulse and rise in blood pressure by 20 mm. systolic and 15 mm. diastolic.

Laboratory Data.—Roentgenograms of the skull showed minimal hyperostosis frontalis interna. A pneumoencephalogram revealed dilated lateral ventricles, with their anterior and posterior horns symmetric in size, shape and position. The third ventricle was also dilated. The cerebral sulci in the frontoparietal regions were dilated. This was interpreted as indicating cortical and subcortical atrophy, particularly in the frontoparietal regions, more pronounced on the left. Spinal tap produced clear fluid, without cells. The Pandy reaction was 1 plus, the Wassermann reaction negative, the colloidal gold curve 12210000 and the total protein 52 mg. per hundred cubic centimeters.

COMMENT

The fluctuation in performance of these patients was particularly evident when complex functions were involved. On some examinations, good contact could be made with the patient, the symptoms were less marked and performance was good. On others, these conditions were reversed. We have found such fluctuation characteristic of all patients with cerebral lesions as contrasted with those with so-called psychogenic manifestations, which are more frequently stable. This fluctuation followed a rhythmic periodicity which was relatively constant for any individual patient, although it differed from one patient to another. The rate of change in performance varied from several minutes (our case 4) to every day (our case 1). Such extraneous factors as attention and distraction, emotional tension, fatigue, irritability and suggestion, altered the performance score at any given moment.[5]

However, there was an inherent cycle of variation independent of these factors. This was proved to our satisfaction by conducting our various perceptual and motor reaction tests in many different

5. Guilford, J. P.: Fluctuation of Attention with Weak Visual Stimuli, Am. J. Psychol. **38**:534, 1927.

circumstances: in a general ward with other patients present and then alone in a small room; forewarning the patient before application of the painful stimulus or applying it suddenly from behind; suggesting a desired reaction or distracting the patient from the test. This observation agrees with experimental evidence of fluctuation of excitability of any cortical point depending on various endogenous stimuli.[6]

All our patients showed a mixed aphasia, with the perceptive and amnestic [7] components predominating. One patient showed important defects initially in the expressive sphere as shown by his inability to pronounce words told him, but it was only as his condition grew worse, when a perceptive aphasia appeared, that his asymbolia for pain manifested itself concurrently. The impairment of integrative or associative capacity was likewise manifested by difficulty in carrying out orders requiring several simultaneous concepts or actions, although simple ones were performed easily.

Spelling of simple monosyllabic words was usually correct, although several trials were frequently necessary. Longer ones could not be spelled at all. Reversal of even the simplest words, such as "cat" or "dog," or of simple series, such as digits or days of the week, was impossible in 3 patients and impaired in the fourth.

Calculation was deficient except when the most elementary sums were involved. The difficulty was more evident for subtraction than for addition or multiplication.

The ability to write, both spontaneously and in copying, was impaired. This varied from inability to reproduce even single letters to the production of a passable semblance of the patient's name. Similarly, copying of simple geometric figures was fairly well done, but Bender's gestalt drawings, which involve spatial orientation, could not be reproduced.

The apraxia present was of the ideokinetic or constructional type, to which Kleist has called attention, manifesting itself in combined or sequential complex actions. Simple acts (such as opening a pin or placing a cigaret in the mouth) could be performed well, either spontaneously or on command.

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6. (*a*) Brown, T. G., and Sherrington, C. S.: On the Instability of a Cortical Point, Proc. Roy Soc. Med. **85**:250, 1912. (*b*) Dusser de Barenne, J. G., and McCulloch, W. S.: An "Extinction" Phenomenon on Stimulation of the Cerebral Cortex, Proc. Soc. Exper. Biol. & Med. **32**:524, 1934. (*c*) Dusser de Barenne, J. G.: Factors for Facilitation and Extinction in the Central Nervous System, J. Neurophysiol. **2**:319, 1939.

7. According to this classification of aphasia, we are interpreting the term "amnestic" as indicating a defect in the associative portion of the speech process whereby the mental image of the word is unavailable and recall and, consequently, verbal reproduction of the word are impossible.

It is evident that the lack of withdrawal seen in these cases might be considered a type of apraxia. But, the expression "pain apraxia" used instead of pain asymbolia would not adequately describe the significance of this symptom. Asymbolia for pain is not only an apractic phenomenon. The inability to carry out a coordinated motor activity is common to both pain asymbolia and apraxia. But even in ideomotor apraxia, considerations of the nature of the stimulus are nonessential. By definition, only the expressive (motor) or integrative arcs are important. In pain asymbolia the concept of painful or unpleasant perceptual experience is just as essential as the motor reaction. It involves a type of behavior toward a particular type of stimulation.

These patients all showed disturbance of their body schema. Some parts of the body could be usually indicated, particularly the nose, eye and ear. The remaining parts could be sometimes designated when their names were given and named when pointed out by the examiner, but errors were frequently made. The most invariable defect was in naming or indicating the named fingers (finger agnosia). Actions involving single parts of the body could usually be performed, but confusion was shown whenever two or more parts were involved. There was no right-left disorientation shown in simple recognition of the sides of the body. Errors were most frequently made in even relatively simple actions requiring a crossing of the midline body axis —for example, left hand to right ear—although a similar action could be performed on the same side. In addition, there was always noticeable hesitation, and frequently there were errors in indication of the examiner's right-left. This spatial disorientation was also evidenced in the inability to reproduce postures involving visuopostural coordination. When a patient's limb was placed by the examiner in a certain position in space, the patient usually had difficulty in placing the corresponding opposite limb in the same position with eyes closed, in spite of the fact that his sense of position and joint movement was intact on passive testing.

It might be objected that in an aphasic patient the degree of agnosia for parts of the body cannot be adequately evaluated in view of the patient's difficulty in understanding or expressing—in other words, that the disorganization of body schema is relative to the aphasia rather than absolute. Such an objection would be applicable only if the aphasia were global. In our cases, it was not marked and was secondary to the amnestic defects. These patients could understand what was said to them and were usually able to indicate some parts but not others, the most constant defect being the finger agnosia.

The symptom complex of finger agnosia, right-left disorientation, acalculia and agraphia has been designated by Gerstmann [8] as a clinical syndrome indicative of a lesion of the gyrus angularis and the adjoining middle occipital circumvolution. This combination was present in our patients with pain asymbolia. If one seeks a purely anatomic localization of function to include both syndromes, this might be predicated on extension of the cortical damage from the angular to the supramarginal gyrus. The constancy of this association would suggest, however, that the two together may be part of a more complete symptom complex, which might contain other components as well. For instance, Schlesinger [9] noted in his own cases and in reviewing the classic case studies of Gerstmann and Mayer-Gross that constructional apraxia was likewise present; this was strikingly so in our own cases. There is adequate clinical evidence of the high degree of dissociability of this complex. Patients with similarly placed lesions of the parieto-occipital cortex will show only one or several of the components and not others. Rather than an expression of loss of function of any isolated cortical zone, this symptomatology must be considered as a pattern of behavior indicating a functional derangement of the total reaction of the body.

The predominant feature shown by our patients was the pain asymbolia, as described by Schilder. The degree of response to the stimulus varied from complete denial of the pain to verbal exclamation after stimulation and finally to some partial movement of escape. Two patients stated repeatedly that the pinprick did not hurt even after prolonged application and to the point of drawing blood. Another would sometimes produce a very inadequate "ouch" when stuck but never any withdrawal or effective reaction of defense. Other stimuli, such as heat or cold, produced a similar result. One patient would hold a lighted match until her fingers would almost burn without dropping it. Special pain-producing tests, including the intravenous injection of histamine and artificially produced muscle ischemia, also provoked the same inadequate response.

Threatening gestures failed equally to produce a protective reaction. For instance, when a pin was brandished before the patient's eyes, there was no blinking, turning of the head, backward withdrawal or defensive movement of the hands. It seemed as though these persons had lost the concept of nocive influences from their environ-

8. Gerstmann, J.: Fingeragnosie und isolierte Agraphie, Ztschr. f. Neurol. **108**:152, 1927.

9. Schlesinger, B.: A Study on Dissociation and Reorganization of Cerebral Function, Confinia neurol. **4**:14, 1946.

ment. Such was not the case, however; if they were menaced verbally, they understood the implication of harmful intention and would respond appropriately.

These phenomena were not absolutely constant. Although present in the great majority of trials, on some occasions there was a response. One patient was extremely irritable at times, and if the painful stimulus was then applied after a verbal menace she would react vigorously. Various observers suggested that the reaction might be due not to the pain-producing pinprick but rather to the emotional threat. Such type of performance would seem to indicate that an increased or decreased state of emotional tension facilitated or decreased the reactivity to pain.

Except for the asymbolia, the other modalities of superficial and deep sensation showed little disturbance. Touch and thermic stimulation were well perceived and to the same extent throughout the body. Passive movements of joints and position of digits in space were normally recognized.

Pain sensation as evaluated by our routine criteria—namely, ability to distinguish between sharp and dull on application of a pointed object or to perceive sharpness with the same intensity—was normal. Subject to the same fluctuations, pinprick was felt as equally sharp wherever applied and distinguished from a blunt stimulus. One patient was thought to be apparently less sensitive to pain over half of his body the day before the appearance of the pain asymbolia. This "hemihypesthesia" may have been a limited form of his asymbolia.

On the contrary, cortical or discriminatory sensation was seriously impaired. There was constant astereognosis as well as inability to recognize texture, smoothness or quality of material touched.

These patients all showed varying degrees of sensory extinction. That it was not constantly present was apparently due to the same periodic fluctuation seen in all the other manifestations.

The presence of a proved focal lesion in the temporoparietal region in all patients showing the asymbolia for pain might lead to the assumption that a "center" for this function exists. Schilder called attention to the proximity of the supramarginal gyrus of the centers subserving the function of body schema orientation on one side and of cortical pain representation on the other.

Such an association appears too mechanistic to be explanatory. The presence of a circumscribed lesion of the cortex does not permit the conclusion that the clinical symptomatology is a manifestation of the loss of a function lying in that area alone. For instance, various clinical syndromes have been ascribed to the supramarginal gyrus. In reporting on a series of patients having bullet wounds of that region, Marie and

Foix [10] described the syndrome of bilateral ideomotor apraxia, global aphasia and right hemisensory impairment with astereognosis but did not note any abnormality in their reaction to painful stimulation. The fragmentation of the parieto-occipital syndrome likewise furnishes ample clinical evidence of this lack of specificity of any particular symptoms for loss of any small cortical area—one of several symptoms of the group being absent in the presence of similarly placed lesions.

In our second patient, in spite of excision of the supramarginal cortex overlying the tumor mass, the pain asymbolia disappeared two weeks later. It would seem that this syndrome is not a manifestation of the destruction of the cortical gray matter per se. Jackson, Fulton and others have pointed out that many clinical symptoms following destructive lesions of the brain cannot be envisaged as simple diminutions of focally represented functions. Frequently they must be considered as normal functions not significantly manifested in ordinary circumstances but becoming exaggerated under pathologic conditions. This has been recently emphasized by Bender [11] in his analysis of sensory symptoms shown after lesions of the parietal and occipital lobes.

Is it necessary to postulate a specificity of function to any particular area of cortical gray matter or to any set of cortical association fibers in order to explain the phenomenon of pain asymbolia? The most that can be admitted is that various motor reactions are integrated in the neighborhood of related sensory areas. Total behavior is dependent on the normal functioning of the entire brain. Any particular manifested abnormal pattern is related to the focal lesion to the extent that destruction of a nodal point of integration will require formation of a new set of reactions by the rest of the brain.

Psychologically it might be said that pain asymbolia results from failure to associate the perceptual experience with the body image, thus producing the inadequate global reaction of the personality. Schilder thus noted that the asymbolia-apraxia was evident only in actions directed against the patient's body. In explanation, he postulated that the postural model of the body became distorted at that point where the painful stimulus was present on its surface.[12] We found no evidence of this localized distortion of the body schema. Our patients did

10. Marie, and Foix, cited by Brock: The Basis of Clinical Neurology, New York, William Wood & Company, 1937, p. 261.

11. (*a*) Bender, M. B.: Changes in Sensory Adaptation Time and After-Sensation with Lesions of the Parietal Lobe, Arch. Neurol. & Psychiat. **55**:299 (April) 1946. (*b*) Bender, M. B., and Teuber, H. L.: Phenomena of Fluctuation, Extinction and Completion in Visual Perception, ibid. **55**:627 (June) 1946.

12. Schilder, P.: The Image and Appearance of the Human Body, London, George Routledge & Sons, Ltd., and Kegan Paul, French, Trubner & Co., Ltd., 1935.

not show any impairment of their ability to localize correctly the point of application of the stimulus on their body. It is rather a loss of the concept of relationship of the body image to its spatial environment and of its integral parts to one another.

Hardy, Wolff and Goodell [13] and Bishop [14] have attempted to dissociate pain sensation into different components, depending on levels of threshold: that of first sensation; that of recognition of sensation as sharp or painful but without emotional protest (the dolorous effect); that of aversion with secondary reaction of avoidance or protection. According to Bishop, this differentiation varies with the successive stages of intensity of stimulation of a given set of "pain" endings and is a continuum. Physiologically, pain asymbolia would correspond to selective loss of the purposeful avoidance-protection response to the highest degree of stimulation. Various drugs have been shown to decrease preponderantly the reaction to pain, with less effect on the threshold of painful perception; certain mental attitudes—distraction, disinterest, apprehension, etc.—may have a comparable effect.

According to the conclusions of these authors, pain asymbolia would be explained on the basis of impaired perceptual acuity, whether due to changes in the brain or to changes in peripheral receptors but on a high threshold. In other words, one cannot apply the pinprick stimulus to the degree sufficient to reach the threshold of pain and withdrawal. But this conclusion would not explain the same lack of reaction to threatening gestures. This viewpoint is a too facile description rather than an explanation of the mechanisms involved. Every perceptual experience of the normal organism carries with it an inherent and inseparable tendency to motor reaction; any dissociation which may occur does so only under specific experimental or pathologic conditions. The physiologic manifestations of body reaction to any external stimulus which is unpleasant or threatening, whether it be physical pain or merely gestures, consist of two groups of phenomena, falling into the "fight or flight" reactions. Objective symptoms, such as pupillary changes, rise in blood pressure, increase in heart rate and simple reflexogenic muscle contractions, do not necessarily require appreciation of the nature of the stimulus.

Subjective manifestations, such as grimacing, verbal exclamation or wincing and more complex "purposeful protective" motor activities, are dependent on the conscious realization of the nocive nature of the stimulus, although they do not require the previous conscious "sensation" of pain.

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13. Hardy, J.; Wolff, H. G., and Goodell, H.: The Pain Threshold in Man, A. Research Nerv. & Ment. Dis., Proc. **23**:1, 1943.

14. Bishop, G. H.: Neural Mechanisms of Cutaneous Sense, Physiol. Rev. **26**:77, 1946.

Reaction to pain necessitates the participation of all levels of the brain, regardless of whether one assumed the cortex or the thalamus to be the central projection of pain sensation. The view of such a conceptual or integrative function as an aggregate of simple neuronal circuits, formed by combination of demarcated sensory or motor "centers" with specific subcortical fibers, is inadequate. These viewpoints must be replaced by more workable theories, such as that advanced by Tower,[15] which sees localization-discrimination (and therefore subsequent reaction) as depending on central "recognition" of the pattern of peripheral activation rather than on a simple pathway involvement.

This is particularly true for perceptual functions. Lashley[16] has gone so far as to state that the gross structural evolution of the nervous system may be largely disregarded when considered in relation to problems of sensory perception. Various psychologic principles have been applied more satisfactorily to explain sensory phenomena in the visual, the auditory and the tactile spheres.

Pain asymbolia, as a type of motor response to a perceptual experience, falls into the same category if this concept is extended to the sensorimotor sphere. Such a viewpoint obviates the apparently necessary discordance between possible pathogeneses of the asymbolia for pain seen in patients with focal cerebral lesions and the abnormal reactions shown by patients with schizophrenia.

The clinical phenomenon of extinction was found in our patients. Just as extinction of pain is a normal phenomenon which has become exaggerated and thus manifested under certain pathologic conditions, so too are varying degrees of reaction to pain seen in normal and in pathologic circumstances. The gamut runs from those persons who react intensely to even slight stimuli to those who permanently show no response to even severe pain (congenital insensitivity).

In general, in the normal person, two simultaneous stimuli inhibit each other (Heyman's law). More specifically, a weak afferent impulse will be diminished by a simultaneous stronger one competing for consciousness in proportion to the quantitative difference between them, even to the point of obliteration of the weaker. In other words, one of the sensations is prevented from passing from its receptive center in the cortex to its nodal center of integration and thence into the rest of the brain required to give it conscious representation. That extinction is present in two simultaneous stimulations of equal intensity, and hypothetically has been attributed to disturbance in the distribution of avail-

15. Tower, S.: Pain: Definition and Properties of the Unit for Sensory Reception, A. Research Nerv. Ment. Dis., Proc. **23**:16, 1943.

16. Lashley, K. S.: The Problem of Cerebral Organization in Vision, Biol. Symposia **7**:301, 1942.

able "nervous energy" between the two hemispheres; the damaged cortex requires more than its usual share, unavailable after the normal cortex has utilized its quota.[11b]

One can only speculate as to exactly what occurs in the pathologic organism to produce pain asymbolia . But this psychologic concept may be advantageously applied to the problem and serves as an adequate theoretic explanation. The reaction to a noxious stimulus also requires transmission of the impulse from the cortical sensory receptive areas to the other parts of the brain participating in the integrated response; the latter includes the "conscious" realization of the pain, the autonomic manifestations and the motor behavior. In purely sensory extinction, a stimulus is so "blocked" that it cannot be further projected along the channels leading to consciousness; in asymbolia for pain, the stimulus is likewise blocked so that it cannot be projected along the channels leading to integrated motor activity. Any explanation based on purely anatomic concepts is inadequate to explain at which level this inhibition occurs. The impairment is not at the cortical sensory level, inasmuch as the pinprick is perceived in a qualitatively and quantitatively accurate manner. Neither is it in the conceptual nor in the purely motor sphere, as verbal threats of injury produce an immediate realiztion of the nocive nature of the stimulus and a consequent adequate posture of defense. The reaction to pain is absent only on the impact of an external, perceptual stimulus, whether visual (threatening gestures) or tactile (pinprick, etc.). Presumably, then, the asymbolia for pain is a phenomenon representing a defect in transcortical or integrative function.

Production of extinction phenomena requires the impingement on the organism of two competitive stimuli. In pain asymbolia, one of these stimuli arriving at the sensory receptive area is enteroceptive, emanating from elsewhere within the organism concurrently with the external impulse. Thus in patients with mental disease occupied with internal complaints, particularly in catatonic patients in whom the role of enteroceptive stimuli is recognized as instrumental in contributing to the psychomotor disturbances, a form of asymbolia for externally applied pain is frequently manifested.[17] This abnormal pain reaction in psychotic patients may be a typical asymbolia.

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17. This was especially striking in one of our cases, that of a 65 year old woman, admitted after a suicidal attempt because of unbearable pain in the legs of eighteen months' duration. Under observation she showed a constant and marked preoccupation with the pain in her leg and various other somatic complaints. Initial neurologic examination revealed decreased knee jerks, absent ankle jerks and absent position and vibratory sensation in her toes; but even

(Footnote continued on next page)

A multiplicity of extraneous impulses are constantly arriving at the sensory receptive area of the cortex, both endogenous and from the environment. The presence of a lesion in the receptive-integrative areas of the dominant cortex so alters the normal sensory circuits that any of these enteroceptive impulses can extinguish the applied stimulus. This hypothesis agrees with the experimental observation by Dusser de Barenne of the rhythmic periodic variation in excitability of any cortical focus, depending on reception of clinically subliminal stimuli from active foci elsewhere in the neuraxis.[18] This mechanism is operative in producing the characteristic fluctuation of all symptoms we observed. In the case of visual extinction described by Bender, his observations corresponded with the hypothesis that the healthy side dominated and inhibited the diseased side . This would appear to hold true in our cases of pain asymbolia. It is significant that in all our cases as well as those reported by Schilder and Stengel the lesion was in the dominant hemi-

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light pinprick caused an immediate withdrawal of her legs and a vigorous protective movement of her hands, with grimacing and moaning. Because of these findings and occasional glycosuria, a tentative diagnosis was made of radiculoneuritis, possibly of diabetic origin, with strong psychogenic exaggeration of pain due to involutional psychosis. All therapeutic efforts to relieve the pain failed, including strong sedation, vitamin therapy, cobra venom, paravertebral block and intravenous injections of procaine hydrochloride. Two months after admission, intraspinal anesthesia was administered, after which the expected motor weakness developed, with areflexia, complete anesthesia up to the level of the first lumbar vertebra and cessation of the pain. The relief persisted about five hours; the following morning the pain was again present, the transitory paraplegia had disappeared, the reflexes were normal and Babinski's sign was found bilaterally. In addition, however, a form of pain asymbolia had appeared. She did not feel painful stimulation up to about the eleventh thoracic vertebra or over her arms up to the shoulders. On her face, chest and upper part of the abdomen, she stated that she felt the pinprick but that it did not hurt. This unusual syndrome progressed rapidly, so that by the following day and during two weeks subsequently a complete asymbolia for pain was present. She felt pinprick everywhere and could distinguish sharp from dull. Superficial touch was normal, as was identification of hot and cold. Localization of the point of application of the stimulus was good. However, on pinprick, even to the point of drawing blood, she disclaimed any pain and would make no reaction of withdrawal of her arms or legs or verbal exclamation. Neither did she react to threatening gestures, as would be expected, by blinking or withdrawing of her hand. There was no aphasia, apraxia or disturbance of body schema.

This abnormal reaction to pain disappeared before the patient's discharge, although her neuropsychiatric symptoms, including the pain in her legs and her somatic preoccupations, remained unchanged. At this time, her nocifensor reactions were again normal. Final neurologic diagnosis was that of posterolateral sclerosis with achlorhydria of undetermined cause.

18. Guilford.[5] Brown and Sherrington.[6a] Dusser de Barenne and McCulloch.[6b]

sphere. The significance of this fact is difficult to evaluate except that it leads to speculation as to whether nocifensor reactions are in some way linked to developmental hemispheric dominance.

SUMMARY AND CONCLUSIONS

Four patients who presented the syndrome of pain asymbolia were studied over a prolonged period. These patients all had lesions of the areas in and around the supramarginal gyrus of the dominant hemisphere proved either at operation or by diagnostic procedures.

The predominant symptom consisted of lack of withdrawal to painful stimuli applied to the body and to threatening gestures. This symptom has been differentiated from a similarly absent or distorted reaction to pain seen in psychotic persons, in those with analgesia due to destructive lesions of the pathways of the neuraxis and in those with congenital insensitivity to pain. Understanding of the significance of the noxious effect of pain was retained, as evidenced by appropriate reaction to verbal menaces. Autonomic reactions were present after application of special pain-producing stimuli (prolonged pinprick, muscle ischemia and intravenous injection of histamine).

Routine neurologic examination showed a normal sensory status according to usual criteria: Pinprick was recognized as sharp; light touch was perceived, and hot and cold were correctly distinguished, equally throughout the body. Stereognosis and discrimination of texture or quality were impaired. The extinction phenomenon for tactile and visual stimuli was found.

These patients had mild degrees of perceptive aphasia and severer amnestic aphasia. In addition, all showed a symptom complex which has classically been considered a deficiency manifestation of lesions of the parieto-occipital region. This included disturbance of body schema as evidenced by right-left disorientation and inability to reproduce postural attitudes in space; Gerstmann's syndrome, or the combination of agraphia, acalculia and finger agnosia; and constructional or idiokinetic apraxia.

The constancy of this symptom complex occurring along with asymbolia for pain and the absence of one or several symptoms of the group in other patients described in the literature as having similarly placed lesions suggests that the symptoms are not merely the expression of loss of function of a center which lies in that relatively small area. The postulated concept of focalization of such a conceptual-integrative function is inadequate. It is felt, rather, that this grouping of symptoms expresses a new pattern of behavior subsequent to a functional reorganization of activity of the entire brain, necessitated by impairment of the integrative role of the parieto-occipital region.

This hypothesis is advanced to explain the mechanism of loss of reaction to nocive stimuli on a psychologic basis, similar to that postulated for the extinction phenomenon. Under normal conditions, the brain is in a state of dynamic equilibrium—or dynamic inactivity—in which it is subject to a constant influx of extraneous endogenous afferent impulses from the viscera, the somatic peripheral receptors or elsewhere in the neuraxis. When the receptive-integrative functions of the parieto-occipital regions are impaired, the pattern of the applied painful stimulus is consequently so altered that it can be obliterated by any of these concomitant enteroceptive impulses. That is, it is psychologically prevented from passing over into the motor sphere, with a resulting appropriate reaction of defense.

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Four patients who presented the syndrome of pain asymbolia were studied over a prolonged period. These patients all had lesions of the areas in and around the supramarginal gyrus of the dominant hemisphere proved either at operation or by diagnostic procedures.

The predominant symptom consisted of lack of withdrawal to painful stimuli applied to the body and to threatening gestures. This symptom has been differentiated from a similarly absent or distorted reaction to pain seen in psychotic persons, in those with analgesia due to destructive lesions of the pathways of the neuraxis and in those with congenital insensitivity to pain. Understanding of the significance of the noxious effect of pain was retained, as evidenced by appropriate reaction to verbal menaces. Autonomic reactions were present after application of special pain-producing stimuli (prolonged pinprick, muscle ischemia and intravenous injection of histamine).

Routine neurologic examination showed a normal sensory status according to usual criteria: Pinprick was recognized as sharp; light touch was perceived, and hot and cold were correctly distinguished, equally throughout the body. Stereognosis and discrimination of texture or quality were impaired. The extinction phenomenon for tactile and visual stimuli was found.

These patients had mild degrees of perceptive aphasia and severer amnestic aphasia. In addition, all showed a symptom complex which has classically been considered a deficiency manifestation of lesions of the parieto-occipital region. This included disturbance of body schema as evidenced by right-left disorientation and inability to reproduce postural attitudes in space; Gerstmann's syndrome, or the combination of agraphia, acalculia and finger agnosia; and constructional or idiokinetic apraxia.

The constancy of this symptom complex occurring along with asymbolia for pain and the absence of one or several symptoms of the group in other patients described in the literature as having similarly placed lesions suggests that the symptoms are not merely the expression of loss of function of a center which lies in that relatively small area. The postulated concept of focalization of such a conceptual-integrative function is inadequate. It is felt, rather, that this grouping of symptoms expresses a new pattern of behavior subsequent to a functional reorganization of activity of the entire brain, necessitated by impairment of the integrative role of the parieto-occipital region.

This hypothesis is advanced to explain the mechanism of loss of reaction to nocive stimuli on a psychologic basis, similar to that postulated for the extinction phenomenon. Under normal conditions, the brain is in a state of dynamic equilibrium—or dynamic inactivity—in which it is subject to a constant influx of extraneous endogenous afferent impulses from the viscera, the somatic peripheral receptors or elsewhere in the neuraxis. When the receptive-integrative functions of the parieto-occipital regions are impaired, the pattern of the applied painful stimulus is consequently so altered that it can be obliterated by any of these concomitant enteroceptive impulses. That is, it is psychologically prevented from passing over into the motor sphere, with a resulting appropriate reaction of defense.

NEUROLOGIC SEQUELAE OF ROCKY MOUNTAIN SPOTTED FEVER

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DURING the acute stage of Rocky Mountain spotted fever the central nervous system is frequently involved. This involvement may be manifested by the clinical findings of confusion, coma, convulsions, hyperactive and pathologic reflexes, cranial nerve palsies, paraplegia and hemiplegia. The most prevalent opinion [1] is that, although these neurologic changes may persist for weeks or months after the onset of the illness, they are usually only transient and ultimately subside without leaving any clinically detectable residuals. Nevertheless, there is evidence that following some acute cases there may remain permanent neurologic sequelae. It is the purpose of this paper to report the clinical and pathologic findings in a case in which disabling neurologic and psychiatric symptoms were maintained for one and one-half years after the onset of Rocky Mountain spotted fever.

REPORT OF A CASE [2]

W. K., a 48 year old white Michigan farmer was well until Aug. 7, 1945, when dizziness, staggering gait, nausea and vomiting developed. One week later he was hospitalized because of severe vertigo, headaches, generalized muscle aching and fever. The essential findings at that time were an oral temperature of 103 F., deafness on the left and stupor. On the fifteenth day of his illness there appeared

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1. (*a*) Wolbach, S. B.: Rocky Mountain Spotted Fever, in Cecil, R. L.: A Textbook of Medicine, ed. 7, Philadelphia, W. B. Saunders Company, 1947, pp. 89-95. (*b*) Queries and Minor Notes, J. A. M. A. **134**:1580 (Aug. 30) 1947. (*c*) Topping, N. H.: Rocky Mountain Spotted Fever, M. Clin. North America **27**:722 (May) 1943. (*d*) Baker, G. E.: Rocky Mountain Spotted Fever, ibid. **28**:752 (May) 1944. (*e*) Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood, and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1945, pp. 476-477. (*f*) Dyer, R. E.: Rickettsial Diseases, J. A. M. A. **124**:1165 (April 22) 1944; correction, ibid. **125**:222 (May 20) 1944.

2. This is the first case of Rocky Mountain spotted fever known to have been contracted in Michigan, and as such has been reported by Dr. G. N. Rein (Rein, G. N.: Rocky Mountain Spotted Fever Appears in Michigan, J. Michigan M. Soc. **47**:182 [Feb.] 1948).

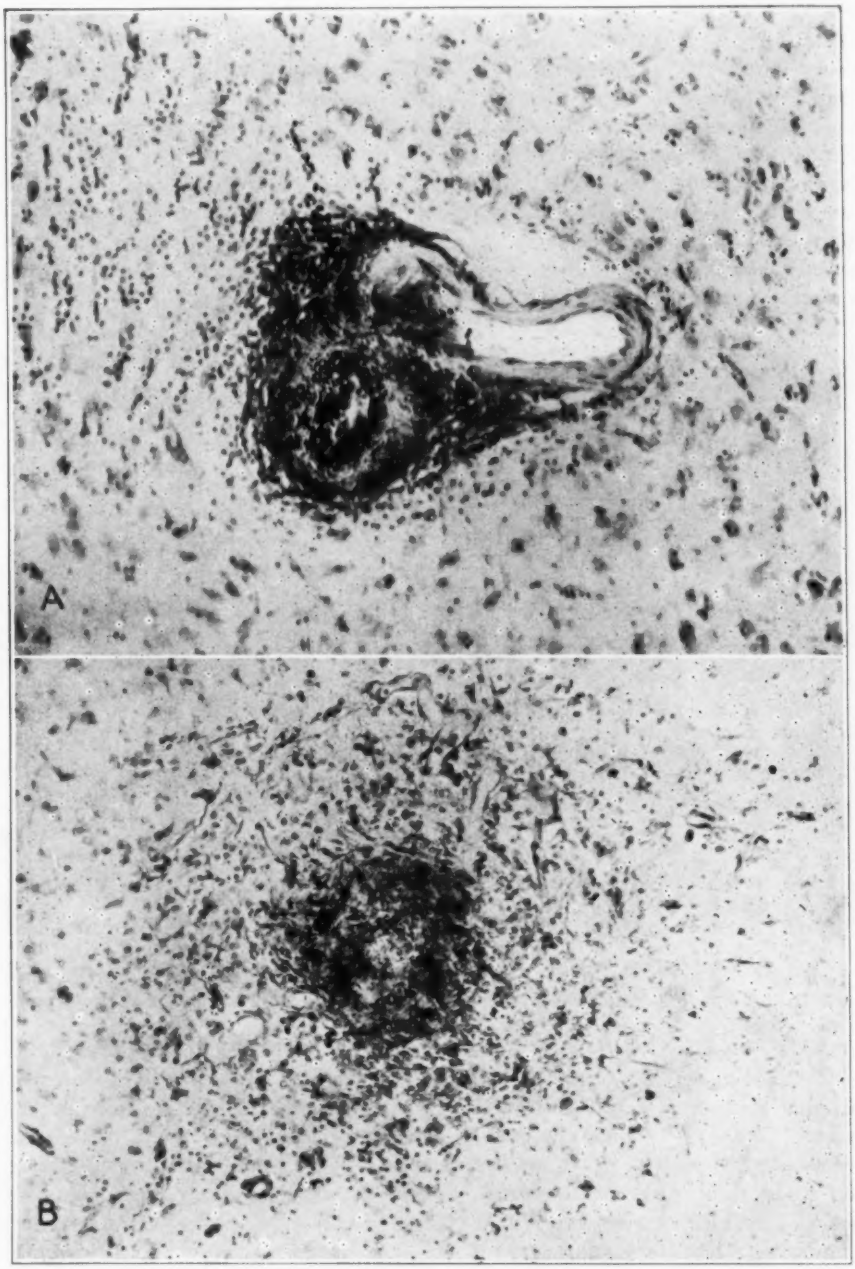

Fig. 1.—The focal lesion of Rocky Mountain spotted fever demonstrated by (*A*) round cell infiltration of the vessel wall and progressive narrowing of the lumen and (*B*) infarction with proliferation of glia in the center and newly formed capillaries at the periphery. Nissl stain; × 150.

an old rose-colored maculopapular eruption about the wrists and ankles. Although there was no history of tick bite, the clinical findings, a complement fixation reaction for Rocky Mountain spotted fever (dilution of 1 : 8,192) and an agglutination of Proteus vulgaris OX_{19} in a dilution of 1 : 1,280 established the diagnosis of Rocky Mountain spotted fever. The patient remained comatose for six weeks despite supportive therapy, which included blood transfusions and administration of penicillin, fluids parenterally and oxygen. During this time his temperature frequently went up to 106 F., and severe decubitus ulcers developed. For several months after regaining consciousness he was unable to recognize members of his family and his speech was unintelligible. He was transformed from a previously "very alert, talkative, ambitious and active" person into one who was "unreliable, forgetful and very quiet." There was also noted a profound weakness of both lower extremities and urinary and fecal incontinence.

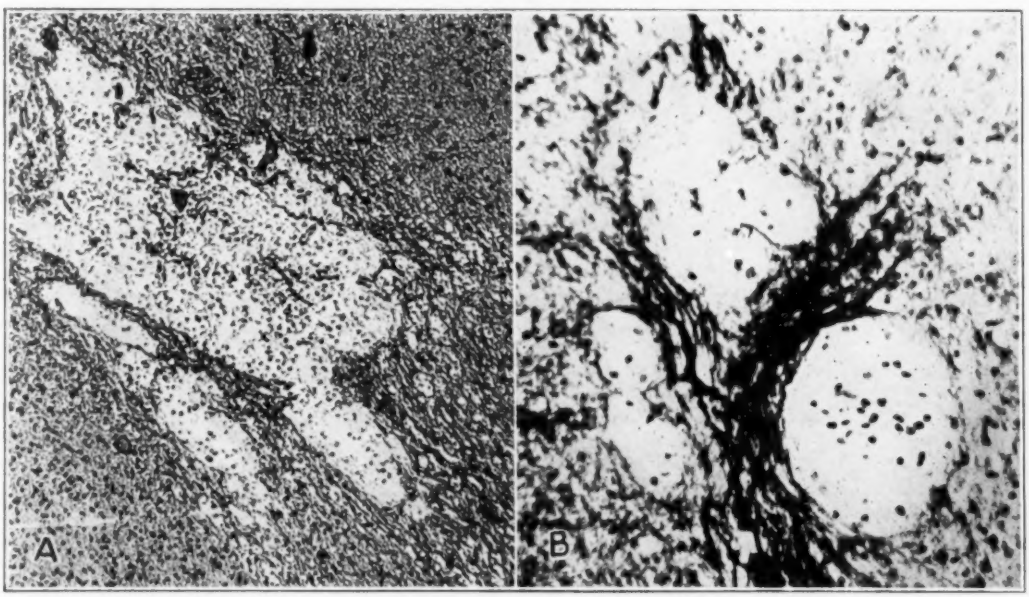

Fig. 2.—*A*, area of old infarction containing numerous gitter cells. Hematoxylin and eosin. *B*, infarcted area surrounded by a thick glial scar. Holzer stain; × 62.

Eighteen months after the onset of his illness he was admitted to the University Hospital, primarily for correction of contractures that had developed in both knees. The only significant abnormalities consisted of decubitus ulcers and severe mental and neurologic disturbances. The mental examination showed him to be disoriented, perseverative, limited in his ability to express ideas and monosyllabic in his responses. His mood was usually euphoric, but at times he was negativistic, belligerent and profane. He was completely unconcerned about his personal appearance, the social amenities and his urinary and fecal incontinence. Psychometric examination revealed a verbal intelligence quotient of 66 on the Wechsler-Bellevue scale. Neurologic examination disclosed clumsiness in the performance of skilled acts, such as lighting a cigaret, and a severe spastic paraplegia with contractures of both knees. Cystometric examination revealed a reflex neurogenic bladder.

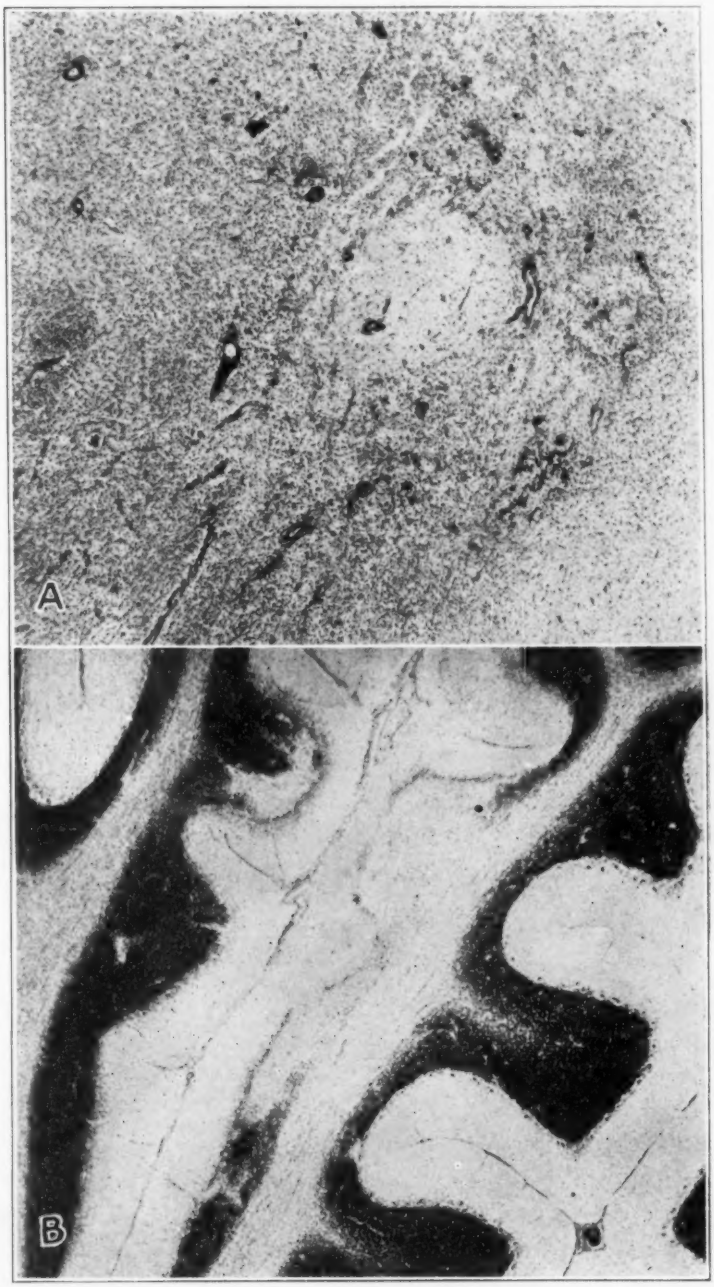

Fig. 3.—*A*, confluent area of softening in the internal capsule which demonstrates the thickened, infiltrated vessels and glial proliferation. *B*, destruction of the cortex of two adjoining cerebellar folia. Nissl stain; Zeiss planar 35 mm.

Agglutination of P vulgaris OX_{19} was still positive in a dilution of 1:160. Roentgenograms of the hips showed changes suggestive of a neurotrophic disturbance on the right and early bilateral coxa mala senilis.

During hospitalization he showed no change in his mental or neurologic status. He died suddenly, nineteen months after the onset of his illness.

Pathologic Report.—The only gross pathologic change in the brain consisted of a 4 mm. brown area of softening in the posterior limb of the right internal capsule. Microscopically, the brain was seen to be affected by focal and diffuse lesions. The basic focal lesion consisted of a microscopic infarct in the vicinity

Fig. 4.—Widespread demyelination and also focal loss of myelin in the internal capsule and middle frontal gyrus. Weigert stain.

of a thickened arteriole. The involved vessels showed a marked proliferation of the intima, a fibrous thickening of the media and adventitia and, at some sites, an accumulation of lymphocytes and monocytes within or surrounding the vessel walls (fig. 1). The lumens of the vessels were narrowed to the point of occlusion by intimal proliferation and mural thrombi. Occasionally there was necrosis of the vessel wall itself. The vascular lesions were surrounded by old infarcts in which both the axons and the myelin were destroyed and replaced by numerous gitter cells containing lipoid and hemosiderin inclusions. The infarcts were

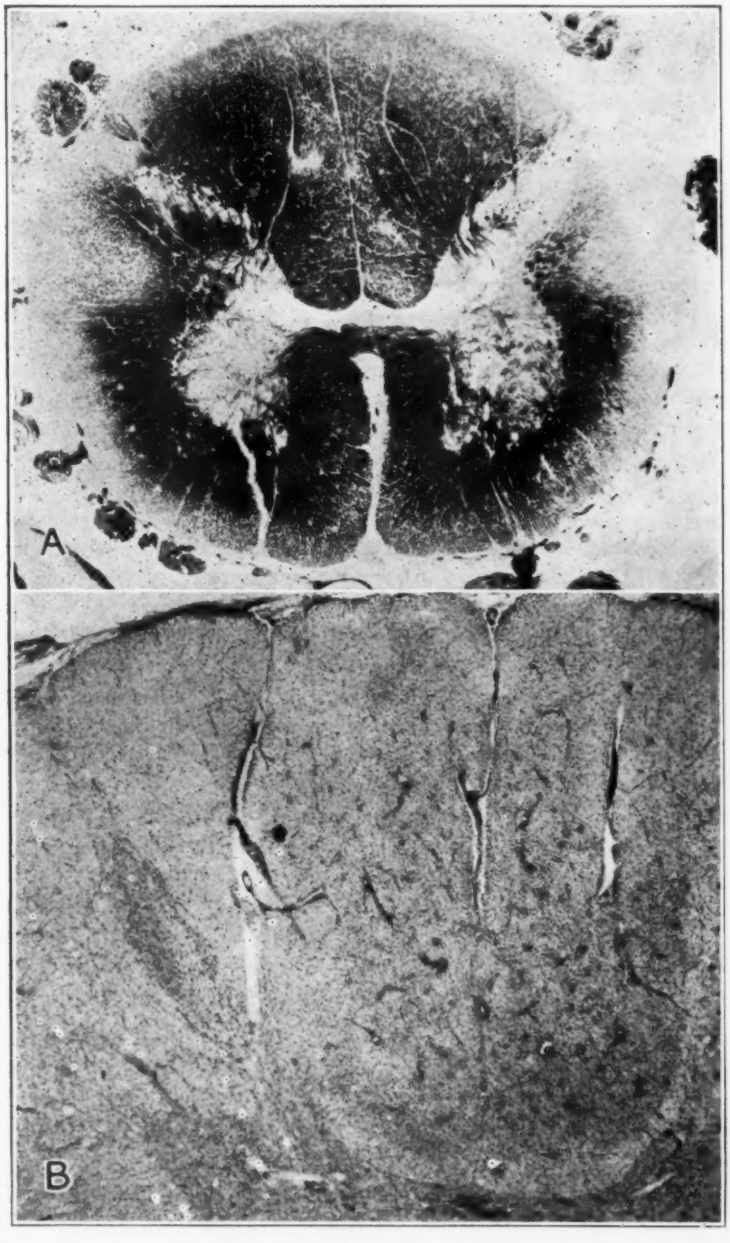

Fig. 5.—*A*, demyelination of the posterior and lateral columns of the spinal cord. Weigert stain; Zeiss planar 75 mm. *B*, vascular thickening and infiltration in the posterior column. Nissl stain; Zeiss planar 35 mm.

encircled by a thick wall of astrocytic fibrils (fig. 2). An infarct of this type was responsible for the single macroscopic softening (fig. 3 *A*). All the other lesions were of microscopic size. They were most numerous in the white matter of the cerebral hemispheres. The stratum radiatum, corpus callosum, fornix and the internal, external and extreme capsules were studded with such microinfarcts. Similar small lesions were present also in the gray matter. In the cerebral cortex they produced a circumscribed loss of neurons. Small lesions were also found in the claustrum, putamen, basis pontis, cerebral peduncles and inferior colliculus. The cerebellar cortex was also severely involved by numerous lesions which destroyed a single or two adjoining folia (fig. 3 *B*).

There was additional diffuse cerebral damage, which was even more extensive than the numerous focal lesions indicated. The cerebral cortex showed some loss of neurons and degenerative changes in the remaining cells. The white matter was affected by a diffuse rarefaction of the myelin in all lobes and concomitant fragmentation of the axons in the same areas (fig. 4). In addition, there was a marked proliferation of astrocytes and microglia in all areas of the white matter, even where the myelin was preserved. This severe glial proliferation was evident in the white matter of the cerebral and cerebellar hemispheres, the fornix and the cerebellar peduncles. The cerebral cortex was also affected by a similar but milder glial proliferation.

The spinal cord showed a severe degeneration of the posterior and lateral columns with associated demyelination and gliosis in these columns (fig. 5 *A*). This was due to the vascular lesions, since there were increased vascularity and thickening of the vessel walls and perivascular accumulation of round cells in the affected columns (fig. 5 *B*). A few small infarcts were seen in the posterior columns and gray matter. The leptomeninges were not significantly involved.

The essential systemic postmortem findings were: focal interstitial myocarditis with multiple microscopic infarcts containing hemosiderin, scar tissue, monocytes and eosinophils; old infarction of the posterior wall of the left ventricle; lipid pneumonitis, and acute edema of the lungs.

COMMENT

Clinical Aspects.—The opinion has been expressed frequently that, although there may be severe involvement of the brain during the acute state of Rocky Mountain spotted fever, if the patient survives these changes are reversed and leave no permanent defect.[3] This is true in most of the cases reported. Some of the reports[4] which offer the opinion that sequelae do occur do not furnish adequate clinical

3. Michie, H. C., Jr., and Parsons, H. H.: Rocky Mountain Spotted Fever, M. Rec. **89**:265 (Feb. 12) 1916. Footnote 1.

4. (*a*) Harrell, G. T.; Venning, W., and Wolff, W. A.: Treatment of Rocky Mountain Spotted Fever, with Particular Reference to Intravenous Fluids: New Approach to Basic Supportive Therapy, J. A. M. A. **126**:929 (Dec. 9) 1944. (*b*) Rubinstein, A. D., and Rowley, A. D.; Endemic Rocky Mountain Spotted Fever, New England J. Med. **229**:455 (Sept. 16) 1945. (*c*) Alpers, B. J.: Clinical Neurology, Philadelphia, F. A. Davis Company, 1946, p. 379. (*d*) Walsh, F. B.: Clinical Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947, p. 618.

data or follow-up studies. Such opinions must be weighed in the light of the evidence that clinical recovery from the neurologic disturbance may occur many months after the onset.[5]

The neurologic defects which persist beyond the acute phase of the disease may be divided into two categories. First, there are those that subside completely in less than one year; second, there are permanent residuals with a known duration of greater than one year. The latter are less common.

Five cases have been reported in which neurologic abnormalities were observed for from two months to one year following the acute illness. In the first case,[5a] a 68 year old woman had prolonged coma and on the thirty-first day right hemiplegia developed, which disappeared within two weeks. Disorientation and mania persisted for over two months after her discharge from the hospital, but within a total of four months the patient had recovered completely.

An 8 year old girl [4b] was comatose for about three months, during which time she had weakness of the left side of the face, dysphagia, absence of voluntary movements and attacks of opisthotonos lasting from a few minutes to a few hours. Within six months after the onset she had regained the ability to talk, stand alone, read and write. The next observation, four years later, indicated complete recovery.

Persistent visual disturbance is reported in the case of a 52 year old white man,[6] who recovered from the acute illness in three weeks but continued to have impaired vision and photophobia for at least three months.

A high degree of hyperesthesia has been reported as persisting for "many months" in 1 instance.[5b]

A 2 year old girl [4a] had convulsions and deep coma during the acute phase of Rocky Mountain spotted fever but responded to supportive therapy. However, she manifested generalized spasticity, mental confusion, choreoathetoid movements, hyperactive reflexes and bilateral Babinski signs for two and one-half months after onset. Although the observers felt that the damage was permanent, there is no report of a subsequent evaluation.

In contrast to these cases in which there was severe neurologic involvement during the acute phase and for several months thereafter, only 2 cases have been reported with known sequelae exceeding one

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5. (*a*) Mulholand, H. B.: Clinical Study of Rocky Mountain Spotted Fever, Eastern Type, Virginia M. Monthly **62**:71 (May) 1935. (*b*) Richards, G. G.: Rocky Mountain Spotted Fever, Ann. Int. Med. **6**:1207 (March) 1933. (*c*) Footnote 4*a* and *b*.

6. Spencer, R. R., and Parker, R. R.: Studies on Rocky Mountain Spotted Fever, Hygienic Laboratory Bulletin 154, United States Treasury Department, Public Health Service, 1930.

year. The first [7] was that of an 8 year old boy who during his illness manifested a left hemiparesis which persisted for four weeks and subsequently caused only some difficulty in walking. Two and one-half months after the onset seizures developed which were confined to the left side of the patient's face. The epileptiform attacks later became generalized and "ran a progressive course with a fatal outcome three years after the onset." There was no report of necropsy observations. The other case [8] was that of a 20 year old white soldier who, after a period of stupor and mental confusion, began to manifest euphoria, hallucinations, incoherence and unreliability, which were still present more than one year after the onset.

It will be noted that the nature of the neurologic sequelae of Rocky Mountain spotted fever fall into five categories: mental changes with diffuse cerebral involvement; convulsive disorder; hemiplegia; paraplegia, and cranial and peripheral nerve involvement. The severer neurologic changes, such as mental abnormality, hemiplegia and paraplegia, usually follow in the wake of a prolonged period of coma or severe systemic illness. Symptoms referable to cranial or peripheral nerves, however, may follow an otherwise relatively benign course.

There appears to be no direct correlation between the severity of the neurologic residuals and the reported changes in the spinal fluid. However, examinations of spinal fluid were seldom repeated even after the appearance of neurologic symptoms.

Pathologic Aspects.—The opinion that the neurologic effects of Rocky Mountain spotted fever are reversible has been encouraged by previous pathologic investigation which has been limited to cases of patients dying from five to twenty-six days after onset.[9] However, the duration of the disease determines, in part, the pathologic findings. In some patients dying within a brief period after onset, there may be no demonstrable lesions in the brain. Patients who survived from

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7. Stroy, H. E.: Rocky Mountain Spotted Fever: Report of Two Iowa Cases with Recovery, J. Iowa M. Soc. **25**:145 (March) 1935; Rocky Mountain Spotted Fever: Report of Three Simultaneous Cases in One Family, ibid. **27**:293 (July) 1937. Jordan, C. F.: Rocky Mountain Spotted Fever and Tick Survey in Iowa, Am. J. Pub. Health **28**:1411 (Dec.) 1938.

8. Palatucci, O. A., and Marangoni, B. A.: Rocky Mountain Spotted Fever, Bull. U. S. Army M. Dept., August 1944, no. 79, p. 116.

9. (*a*) Wolbach, S. B.: Studies on Rocky Mountain Spotted Fever, J. M. Research **41**:1 (Nov.) 1919. (*b*) Lillie, R. D.: Pathology of Rocky Mountain Spotted Fever, National Institute of Health Bulletin 177, Federal Security Agency, United States Public Health Service, 1941. (*c*) Hassin, G. B.: Cerebral Changes in Rocky Mountain Spotted Fever, Arch. Neurol. & Psychiat. **44**:1290 (Dec.) 1940. (*d*) Scheinker, I. M.: Histologic Observations on the Changes in the Brain in Rocky Mountain Spotted Fever, Arch. Path. **35**:583 (April) 1943.

five [9d] to eleven [9c] days showed only moderate vascular and glial reactions, even though the causative organism was found within the endothelial cells.[9a] The characteristic thrombonecrotic lesions have been demonstrable consistently only after the infection had persisted for at least twelve days.[9b]

The typical lesions [10] develop from swelling and proliferation of the endothelium of the small vessels, infiltration of the vessel walls by round cells, and formation of hyaline and karyorrhectic cellular thrombi. The resulting thromboses produce numerous microinfarcts and some small hemorrhagic extravasations. There is frequently a perivascular proliferation of glia. The oldest lesions show clear spaces, into which there is a proliferation of capillaries from the periphery. However, this type of lesion represents the pathologic change as it occurs in the acute cases. If the patient survives an attack that is of considerable duration and severity, it might be anticipated that the lesion found at a later date would represent old healed vascular lesions. Such changes were encountered in our case in the form of thickened or thrombosed vessels, old organized infarcts surrounded by gitter cells and glial scars, and evidence of previous hemorrhagic extravasations. But, corresponding to the profound neurologic and psychiatric sequelae, the involvement of the cerebral parenchyma was even more extensive and not confined merely to the sites of the numerous disseminated vascular lesions. Instead, additional diffuse destruction was also evident in the widespread demyelination and even better demonstrated by the intense proliferation of astrocytes and microglia throughout the entire white matter, even where the myelin was preserved.

SUMMARY

Although the involvement of the central nervous system in Rocky Mountain spotted fever usually either is followed by complete recovery or results in death during the acute stage, in rare cases significant neurologic sequelae may remain. The nature of the sequelae has been obscure because pathologic observations have heretofore been confined to cases in which death occurred during the acute phase.

A case is reported in which an acute course was followed by pronounced mental deterioration and a spastic paraplegia which persisted for nineteen months without recovery. Pathologic study of the brain revealed numerous old thrombonecrotic lesions and microinfarcts. In addition, there were widespread demyelination and an intense proliferation of glia in all parts of the white matter. The posterior and lateral columns of the spinal cord were similarly affected.

10. Topping.[1c] Baker.[1d] Lillie.[9b]

"INVERTED MARCUS GUNN PHENOMENON"

(So-Called Marin Amat Syndrome)

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SAN FRANCISCO

THE ASSOCIATED movement between the jaw and the upper eyelid described first by the London ophthalmologist Marcus Gunn in 1883 evoked great interest among neurologists and ophthalmologists. There have been many publications on this subject, even in recent years. This phenomenon, usually called jaw-winking phenomenon, consists of automatic, involuntary, irresistible lifting of the ptotic eyelid when the mouth is opened, and particularly when the mandible is moved to the side opposite the ptosis. Of the numerous modifications of the original Marcus Gunn phenomenon described in the voluminous international literature, the so-called inverted Marcus Gunn phenomenon is of great physiologic interest. In this condition, on movement of the mandible, not a lifting of the eyelid but a closure of the eye occurs.

Since the phenomenon of Marcus Gunn has been so often observed and thoroughly investigated, one is from the very outset justified in being skeptical of the existence of the rarely seen inverted form. None of the many theories on the physiologic mechanism of this phenomenon could offer an explanation for both forms.

My unforgettable teacher William Spiller in Philadelphia in 1926 once said to me: "Do not try to explain anything that may be wrong in the first place." This simple, ingenious rule has proved very fruitful to me in countless instances. With this point of view in mind, it is worth while to review critically the cases of so-called inverted Marcus Gunn phenomenon.

In an article written in Spanish in 1918[1] and translated into French in 1919[2] Marin Amat described a phenomenon which he "had not found described before." In 1 case he observed very clearly perceptible involuntary contractions of the right orbicularis oculi muscle synergic with movement of the mandible. He concluded that this was

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1. Marin Amat: Contribución al estudio de la curabilidad de las parálisis oculares de origen traumático, Arch. oftal. hispano-am., 1918, p. 71.

2. Marin Amat: Sur le syndrome ou phénomène de Marcus Gunn, Ann. d'ocul. **156**:513, 1919.

a "syndrome of inverted Marcus Gunn." In 1932 Coppez [3] suggested the name "Marin Amat syndrome" [4] for this phenomenon.

The new syndrome found considerable interest. Villard [5] called the case of Marin Amat "probably unique." Referring to abnormal forms of the Marcus Gunn phenomenon and to the work of Marin Amat, Charamis [6] spoke of "still more paradoxical and more complicated cases of Marcus Gunn phenomenon." In the literature—for instance, in the monumental French "Traité d' ophthalmologie" [7] the syndrome of Marin Amat is mentioned after that of Marcus Gunn. In the most recent review on the synkineses of the muscles of the cranial nerves (1944) Streiff [8] listed, after the original Marcus Gunn phenomenon, "inverted Marcus Gunn" : dropping of eyelid on movement of lower jaw. However, closure of the eye on movement of the mandible had been described long before Marin Amat—in 1894 by Müller-Kannberg [9] and in 1902 by Higier.[10]

The case described by Marin Amat,[1] to which he referred in later publications,[11] was that of a 56 year old man. When the patient started to chew, tears flowed from his right eye, and the eye closed automatically when he opened his mouth or while chewing. Marin Amat saw in this phenomenon an associated movement between the trigeminal and the facial nerves.

In 1926, the French ophthalmologist Benoit,[12] who had translated the original Spanish article of Marin Amat, referring to this case, de-

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3. Coppez, H.: (*a*) Le syndrome de Marin Amat, Bull. Soc. belge d'opht. **65**:88, 1932; (*b*) Quelques cas rares de syncinésie oculaire, Rev. oto-neuro-opht. **11**:503, 1933.

4. In some publications this author is referred to as "Amat," and the term "Amat syndrome" is used. This is not correct, since the family name of this Spanish ophthalmologist is Marin Amat, his given name Manuel.

5. Villard, H.: Le phénomène de Marcus Gunn, Arch. d'opht. **42**:513, 1925.

6. Charamis, J. S.: Formes anormales du phénomène de Marcus Gunn, Arch. d'opht. **46**:663, 1929.

7. Jean-Sédan: Trouble de l'appareil moteur des paupières, in Bailliart, P.; Coutela, C.; Redslob, E., and Velter, E.: Traité d'ophthalomologie, Paris, Masson & Cie, 1939, vol. 3, p. 1073.

8. Streiff, E. B.: Syncinésie palpébro-nasale, Confinia neurol. **6**:215, 1944-1945.

9. Müller-Kannberg: Eigentümliche Mitbewegung eines ptotischen Lides bei Unterkieferbewegungen, Ärzt. Prakt. **7**:1177, 1894.

10. Higier, H.: Zur Klinik der eigenthümlichen Mitbewegungen des paretischen Lidhebers und Lidschliessers, Deutsche Ztschr. f. Nervenh. **21**:306, 1902.

11. (*a*) Marin Amat, M.: Acerca del denominado por nosotros sindrome o fenómeno de Marcus Gunn, invertido, Gac. méd. españ., 1928, p. 487; (*b*) Sobre un nuevo caso de "Sindrome o Fenómeno de Marcus Gunn," Siglo med. **86**:57 (July 19) 1930; (*c*) in discussion of Coppez.[17]

12. Benoit, M.: Syndrome inversé de Marcus Gunn, Soc. d'opht. Paris, 1926, p. 269.

scribed a woman of 49 who showed the same phenomenon: When the patient opened her mouth or when she laughed, the left palpebral fissure closed by itself. This occurred only when she opened her mouth forcefully. "When the patient half opened her mouth, nothing abnormal happened." Benoit assumed, as did Marin Amat, that a peripheral anastomosis existed here "without a doubt" between the fifth and the seventh nerve, whereas—according to Benoit—"Marcus Gunn phenomenon might be due to connections situated centrally."

Coppez,[3a] the leading Belgian ophthalmologist of his time, in 1932 said:

> . . . We have recently published an article on the classification of the ocular synkineses. Now we want to complete this work by the study of a rarely observed synkinesis between the facial nerve and the motor branch of the trigeminus. This synkinesis was described for the first time by Marin Amat under the name of inverted Marcus Gunn syndrome. We gladly propose the name "Syndrome of Marin Amat" which seems justified.

Coppez added another case. A girl of 15 years showed contraction of the left orbicularis oculi muscle on mastication. This contraction was synchronous with the movement of the lower jaw. This is due—said Coppez—to a synkinesis between some fibers of the facial, and some of the motor trigeminus, nerve.

Referring to this report of Coppez, Zenan [13] offered another "case of Marin Amat syndrome." Opening of the mouth, chewing, was accompanied with spasmodic contractions of the right orbicularis oculi in a woman of 41 years. "The phenomenon occurred with such frequency as to render the life of the patient intolerable." Zenan classified this condition as "ocular synkinesis, type Marin Amat." As in the cases of Marin Amat, Benoit and Coppez, movement of the lower jaw brought forth clonic contractions of the orbicularis oculi muscle. Zenan postulated a nervous motor stimulus, emanating from the masticatory nucleus and reaching the nucleus of the superior facial nerve by a true short circuit.

In 1944, without reference to similar cases previously described, Halpern [14] reported 4 cases which showed "a correlation of movements between eyelid and mandible." The reader is left with the impression that a completely new phenomenon was described by Halpern. In all these cases "movement of the jaw caused not, as in the original Gunn phenomenon, opening, but closure of the eyelid." "The inverted Gunn phenomenon," as Halpern calls it, occurred here

13. Zanen, J.: Un cas de syndrome de Marin-Amat, Bull. Soc. belge d'opht. **67**:75, 1934.

14. Halpern, L.: (*a*) Zur Phänomenologie einer motorischen Korrelation zwischen Lid und Kiefer, Schweiz. Arch. f. Neurol. u. Psychiat. **54**:134-141, 1944; (*b*) The Inverted Gunn Phenomenon, Acta med. orient. **4**:342, 1945.

. . . (1) on voluntary opening of the mouth, (2) during voluntary chewing, (3) during the unvoluntary process of yawning, and (4) during the emotional process of laughing. . . . While in the case of the Gunn phenomenon the correlation is between the motor function of the jaw and the oculomotorius nerve, this correlation is one of the motor function of the jaw, on the one hand, of the facial nerve, on the other.

Halpern assumed that this phenomenon is supranuclear in origin.

Streiff [8] listed "inverted Marcus Gunn" under the heading of synkinesis between the fifth and third nerves. This is not correct, since closure of the eye is a function of the seventh and not of the third nerve.

In all these cases the so-called inverted Marcus Gunn phenomenon existed on one side of the face only. In the literature 2 cases are reported in which on one side of the face the phenomenon as originally described by Marcus Gunn existed, while the other side showed the inverted form of this phenomenon. In 1894 Müller-Kannberg [9] reported the case of a 12 year old girl who showed ptosis and Marcus Gunn phenomenon on the left side. When she opened the mouth, the left-sided ptosis disappeared but at the same time the right eye closed. In 1902 Higier [10] described a patient of 32 years who had a congenital ptosis with a typical Marcus Gunn phenomenon on the right side. On the left side he had no ptosis; on the contrary, the orbital fissure was wider than normal. When the patient started to chew, the right eye opened, as in the Marcus Gunn phenomenon, but the left eye closed.

The descriptions of the inverted Marcus Gunn phenomenon of some of the authors mentioned were accompanied with illustrations. One of these, that of Halpern, is reproduced here. Figure 1*A* shows the normal position of the lid when the mouth is closed; figure 1*B* shows the reflex closure of the eyelid on opening of the mouth. Looking at these pictures, one is instantly struck by the fact that this automatic closure of the homolateral eyelid is seen in cases of partial recovery from facial palsy in which contractures and associated movements exist. One is reminded that these associated movements commonly, easily and markedly involve the orbicularis oculi muscle. Schirmer,[15] for instance, described the case of a man of 28 years, in whom a left-sided facial paralysis developed. After seven months, except for a slight weakness of the facial muscles, the recovery was perfect, but then associated movements set in. "Every movement of his left cheek [in laughing and chewing] is accompanied by a partial closure of his left eyelid." This must be regarded as typical. This unmistakable and striking similarity of movement, this same great responsiveness of the orbicularis oculi seen in the two conditions,

15. Schirmer, O.: Associated Movements of the Eyelids, Arch. Ophth. **46:** 169, 1917.

naturally raises the question as to whether they are identical, and thus the movement as observed in Marin Amat syndrome is nothing else but one of the numerous associated movements observed in old facial palsy. If this is the case, patients with Marin Amat syndrome must have a history of a previously sustained facial palsy or must present some findings indicating the remnants of such a palsy, like weakness, contractures, associated movements among other components of the facial musculature or the so-called gustolacrimal reflex: flow of tears from the eye on the affected side when gustatory stimuli reach the anterior part of the tongue. It might be worth while mentioning that weakness of the muscles is not a *conditio sine qua non* for appearance of associated movements after facial palsy; these may exist

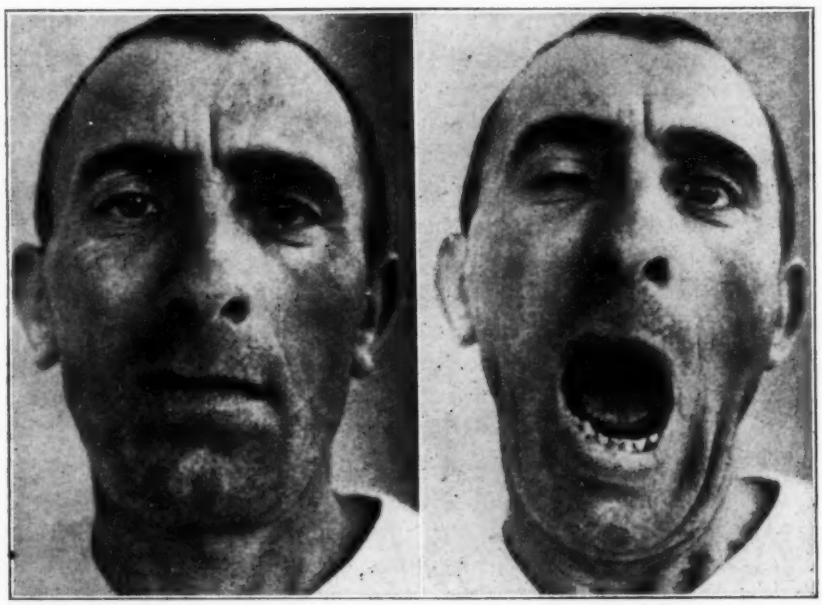

Fig. 1.—"Inverted Marcus Gunn phenomenon." *A*, normal position of the lid when the mouth is closed; *B*, reflex closure of the eyelid on opening of the mouth. (From Halpern,[14a] p. 135).

without facial palsy, as in facial hemispasm (Wartenberg [15a]) or when recovery from palsy is complete.

From this point of view let us critically consider the history and findings in cases of inverted Marcus Gunn phenomenon, cases which have been called "unique" or "paradoxic." A recheck of all the reported cases revealed that in every one of them a facial palsy preceded the appearance of the "inverted Marcus Gunn." In the original case described by Marin Amat, which led to the introduction of the

15a. Wartenberg, R.: Associated Movements in the Oculomotor and Facial Muscles, Arch. Neurol. & Psychiat. **55**:439 (May) 1946.

syndrome which bears his name, there previously had been a traumatic right-sided facial palsy due to skull fracture. An examination a year and a half after the injury revealed that the strength and the tonus of the affected muscles had returned to normal. The patient showed in outspoken form the gustolacrimal reflex sometimes seen after peripheral facial palsy. "When the patient started to masticate," said Marin Amat, "tears flowed without interruption down his cheek."

> . . . But still more bizarre [in another place Marin Amat says "astounding"] is the phenomenon which we have not found described before. One sees involuntary, very perceptible, contractions of the fibers of the right orbicularis oculi synergic with the movement of the lower jaw. When the lower jaw drops, the lower lid rises, and the upper lid descends." Referring to the same case in 1932, Marin Amat [11c] said: "When the patient opened his mouth for mastication, true or simulated, orbicularis oculi and *other facial muscles* on the right side contracted." (italics mine.)

The patient of Benoit [12] with the "inverted Marcus Gunn" syndrome had "classic signs" of a left-sided facial paralysis *a frigore*. Later, contractures of the muscles of the affected side developed. The strength of the orbicularis oculi was restored. The author described mass associated movements of the affected facial muscles: When the patient tries to close the left eye, "one sees all the superficial muscles of the left side contract." The author continues to describe all the typical motor phenomena of associated movements after incomplete recovery from peripheral facial palsy.

> . . . When the patient half opens her mouth, nothing abnormal takes place, but when she drops her jaw forcefully, . . . one sees the left upper lid fall. Even during normal conversation one could see slight twitching in the left upper lid. Contraction of the pterygoidus externus muscle is of no influence on the phenomenon of the upper lid. Neither is the forcible innervation of the masseter while the mouth is closed. On laughing, on muscle strain, on coughing, on yawning the eye lid closes.

Despite this description of clearcut intrafacial associated movements, Benoit assumes an anastomosis between the trigeminal and facial nerves.

The case of Coppez,[8] which induced him to establish the "syndrome of Marin Amat," was that of a young girl with right-sided paralysis of the facial nerve *a frigore*. She improved after a year, but contractures of the affected muscles followed. "When she laughs, the right-sided orbicularis oculi muscle contracts by successive twitchings, and the eyelids finally close." This, said Coppez, is a "facial synkinesis." "When the patient chews, the orbicularis oculi is the site of contractions which are synchronous with the movements of mastication." This too, said Coppez, is a synkinesis but between the branches of the facial and the motor trigeminus nerve.

The meager description of the case of Zanen [13] leads one to suppose that the patient may have had a syphilitic facial paralysis of the right side. It is noteworthy that for two months she had had "clonic spasms" of the right orbicularis oculi not only on mastication but also on laughing or simply opening the mouth.

In the first case of Halpern [14] the patient had a right-sided peripheral facial palsy, which in the course of four years had slowly subsided. Oddly enough, in two articles on the subject, Halpern noted no motor phenomena of the facial muscles other than automatic closure of the eye on opening of the mouth. In his second case, too, there was a left-sided peripheral facial palsy, which after five months had completely subsided. The movements of the lids became normal. But for three months the patient closed the left eye automatically when she started to chew. On mere movement of the mandible without the act of real eating, this phenomenon did not appear. Here, too, no other phenomena in the area of the facial muscles were noted. In his third case, a young man with left-sided rheumatic facial paralysis showed fairly good recovery after a few months. In this case no closure of the eyelid took place on opening of the mouth or on chewing, but closure did appear on yawning. In the fourth case a patient with peripheral facial palsy, which after two years had shown marked improvement, manifested an "inverted Marcus Gunn phenomenon" but not on opening of the mouth, on chewing or on yawning. The phenomenon appeared only on spontaneous laughing. The experience, said Halpern, taught him that this phenomenon usually develops after complete or at least functional recovery from facial palsy.

In the cases mentioned, there was a Marin Amat syndrome on one side of the face while the other side was normal. Two cases have been reported in the literature, by Müller-Kannberg [9] and Higier,[10] respectively, which showed Marcus Gunn phenomenon on one side of the face and Marin Amat phenomenon on the other. When the patient opened his mouth, one eyelid rose while the other eyelid dropped! The case of Müller-Kannberg was that of a 12 year old girl. The author did not mention specifically the name of Marcus Gunn, but from his description there can be no doubt that the patient showed this phenomenon on the left side. Particularly pathognomonic was the rising of the ptotic lid on movement of the mandible to the right. But, while lowering of the jaw and its movement to the right caused the ptotic lid to rise, it also caused the right lid to drop. Unfortunately, there is not a single word in this report regarding the status of the facial muscles on the right side. Therefore, for the present discussion this report is of no value.

The patient of Higier, a man of 32 years, with Marin Amat syndrome on the left side, had had facial paralysis on that side nine

months previously. He had a paresis of the left orbicularis oculi with lagophthalmos. Higier described how involuntary associated movements appeared in the paretic facial muscles. On eating, or laughing and on showing the teeth, the left lid contracted until the eye was completely closed. On movement of the left corner of the mouth and on opening of the mouth the left eye closed too.

Unfortunately, the neurologic examination in most of these cases is incomplete and inadequate. The authors—mostly ophthalmologists—in their enthusiasm over the discovery of the new phenomenon (closure of the eye on opening of the mouth) stopped right there. They failed to search for other intrafacial associated movements and to prove by meticulous examination that it is the exclusive movement of the trigeminal muscles that brings about the closure of the eye. However, what they did describe speaks a neurologic language clear enough to interpret this phenomenon correctly. This description, though meager, allows one to assume that the patients with Marin Amat syndrome had peripheral facial palsy, and in most of them associated movements developed after incomplete recovery from this palsy. In some cases recovery was apparently complete; some showed the gustolacrimal reflex, often seen in old facial palsy.

To understand the Marin Amat syndrome which these patients show—i. e., closure of the eye on opening of the mouth—one must realize that associated movements after recovery from facial palsy may be very extensive and intensive. They are extensive because they involve all the components of the facial musculature. The principle of this group now is "all for one." The slightest impulse sent to any of these muscles is transmitted to all the others, even the most remote. The unit acts *in toto*. Since Hitzig,[16] in 1872, first drew attention to the synkinetic movements of the facial muscles, many attempts to describe individual types of these movements have been made. Each type appeared so important to its discoverer and to the champion who reviewed it later that many a type is catalogued carrying the burden of the name of the man who first described it. Coppez,[17] for instance, referred to the following types: palpebro-buccal (Debove,[18] Achard[19]), palpebro-bucco-frontal (Lamy[20]), palpebro-

16. Hitzig, E.: Ueber die Auffassung einiger Anomalieen der Muskelinnervation, Arch. f. Psychiat. **3**:312 and 601, 1872.

17. Coppez, H.: Quelques cas de syncinésies oculaires, Bull. et mém. Soc. franç. d'opht. **45**:411, 1932.

18. Debove: Des mouvements associés dans la paralysie faciale, Bull. et mém. Soc. méd. d. hôp. de Paris **3**:119, 1891.

19. Achard: Mouvements associés dans la paralysie faciale, Gaz. d' hôp. **64**: 673, 1891.

20. Lamy, H.: Contractions "synergiques paradoxales" observées a la suite de le paralysie faciale périphérique, Nouv. iconog. de la Salpêtrière **18**:424, 1905.

platysmal (Lévy [21]), palpebro-auricular (Rendu [22]). Streiff [8] lists ten different pathologic synkinesias among the various facial muscles. Even this list could be extended! This, however, would serve no useful purpose, nor does the attachment of proper names to the various types. The fact of the matter is that in acting "all for one" every one of the facial muscles participates mutually in their play. Hence, the great variety of possible combinations. All the more so, since not all the muscles respond with equal readiness and strength to the call of other muscles. It is an indisputable clinical fact that the orbicularis oculi shows the greatest responsiveness to the innervation of other muscles, especially those which innervate the corner of the mouth. The reason may be a physiologic one, protection of the eye, or it may simply be that the contractions of these muscles are more easily visible.

In any event, viewing the associated movements of the facial muscles which occur after incomplete recovery from facial palsy, one is struck by the ease and strength with which the orbicularis oculi responds to any action of any other muscle. One is compelled to say that, whatever the patient does, or tries to do, with any facial muscle, he inevitably closes his eye. The high degree of responsiveness which the orbicularis oculi shows is best documented by its relationship to the remote platysma muscle. When associated movements of the facial muscles exist and the patient innervates the platysma muscle alone—which can be accomplished after repeated trials—he automatically closes his eye on the diseased side. And this relationship is also reversed; on forcible closure of the eye, the platysma muscle may respond partially. The following phenomenon is remarkable in this respect. On elicitation of the orbicularis oculi reflex by tapping in the neighborhood of this muscle, and thus evoking closure of the eye, one can see simultaneous contraction of a strand of the platysma muscle on the medial aspect of the platysma under the chin. This is a movement of the platysma associated with the reflex movement of the orbicularis oculi.

Considering all this, it is clear that on opening of the mouth, especially on forceful opening, a patient with associated movements after facial palsy, which may or may not have left demonstrable weakness of the facial muscles, must innervate some facial muscles. The opening of the mouth especially affects the orbicularis oris and the numerous muscles more or less closely or loosely connected with it, all of which are innervated by the facial nerve. It is hardly possible

21. Lévy: Deux cas de paralysie faciale périphérique avec participation du peaucier, Bull. et mém. Soc. méd. d. hôp. de Paris **42**:177, 1918.

22. Rendu, R.: Syncinésie auriculo-palpébrale dans la paralysie faciale, Rev. de laryng. **43**:977, 1922.

to open the mouth without innervating some muscles of the lower part of the face. If this is so, then the innervation of these lower facial muscles must bring about an associated movement of the orbicularis oculi. This is all the more understandable since it is known how susceptible and sensitive this muscle is, how extremely responsive and how readily it participates in any action of the neighboring muscles.

Though it is thus evident that the so-called Marin Amat syndrome is nothing else but a common intrafacial associated movement and not a trigeminofacial movement, 8 patients with associated movements of the facial muscles have been rechecked critically to verify this. On careful examination it has been found in every case without exception that:

(1) Movement of the mandible itself—either opening or closing of the mouth or lateral deviation—even when such a movement is performed forcefully or against resistence, has no effect on the orbicularis oculi. This obtains only so long as no other—i. e. facial—muscles become involved.

(2) When the range of the movement of the mandible becomes so extensive that the facial muscles are involved secondarily, the orbicularis oculi comes into play with alacrity.

(3) Observing these associated movements, one gains the definite impression that the action of the orbicularis oculi, the closing of the eye, is contingent on action of other facial muscles and not on the action of the trigeminal muscles.

The following cases illustrate some points under discussion.

REPORT OF CASES

CASE 1 (fig. 2).—A 35 year old man had facial palsy on the right after operation on the mastoid five years before. Functional recovery has been almost complete, but there are associated movements among the facial muscles. Figure 2, *A*, shows the face at rest. Hardly any anomaly can be seen. Figure 2, *B*, shows the face when the patient was asked to broaden his mouth slightly and slowly. It was very striking that, despite the mildness of the primary movement, there was a complete involuntary closure of the homolateral eye simultaneously. The latter movement was considerably greater in strength and range than the primary movement of the lips.

CASE 2 (fig. 3).—A 50 year old man has had right-sided facial hemispasm for three years. This case has been discussed elsewhere and from another standpoint (Wartenberg [15a]). The hemifacial spasm was the only objective pathologic sign except for associated movements of the facial muscles on the same side. I have found such associated movements present in every case of so-called cryptogenic hemifacial spasm which I have observed, and these associated movements were mostly unnoticed by the patients, even when such a condition had persisted for many years. Illustrations (Wartenberg,[15a] p. 463) show these mutual associated

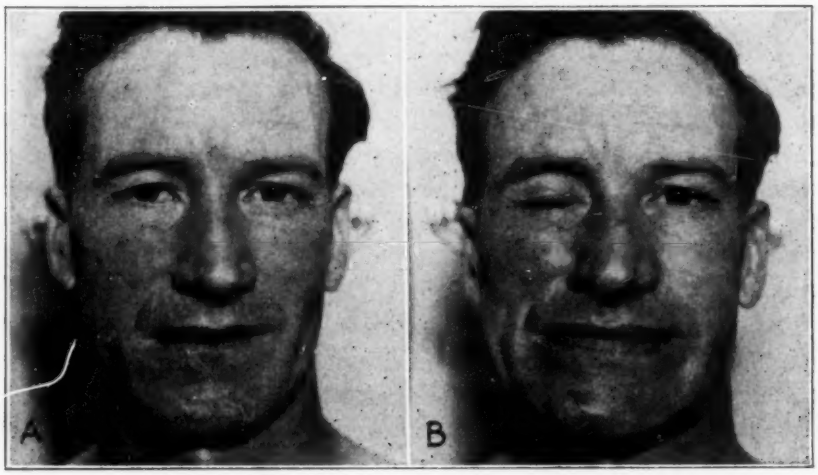

Fig. 2 (case 1).—Old right-sided peripheral facial palsy with good functional recovery but with associated movements among the facial muscles. *A*, face of the patient at rest; *B*, marked associated movement of the right orbicularis oculi on slight innervation of the corner of the mouth.

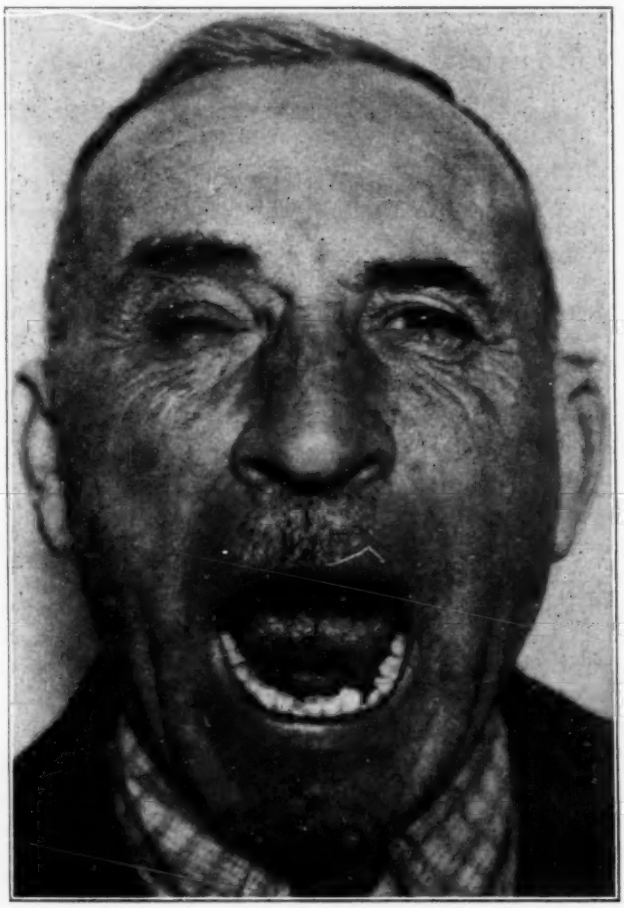

Fig. 3 (case 2).—Right-sided cryptogenic hemifacial spasm with intrafacial associated movements; closure of the eye on the affected side on forceful wide opening of the mouth. (For other photographs of this patient, see Wartenberg,[15a] p. 463.)

movements between the movers of the corners of the mouth and the closers of the eye. In this case, as in case 1 of this series, it is remarkable that the face of the patient at rest shows no anomaly. The striking closure of the eye on the same side as the spasm on forceful wide opening of the mouth is seen in figure 3. There were

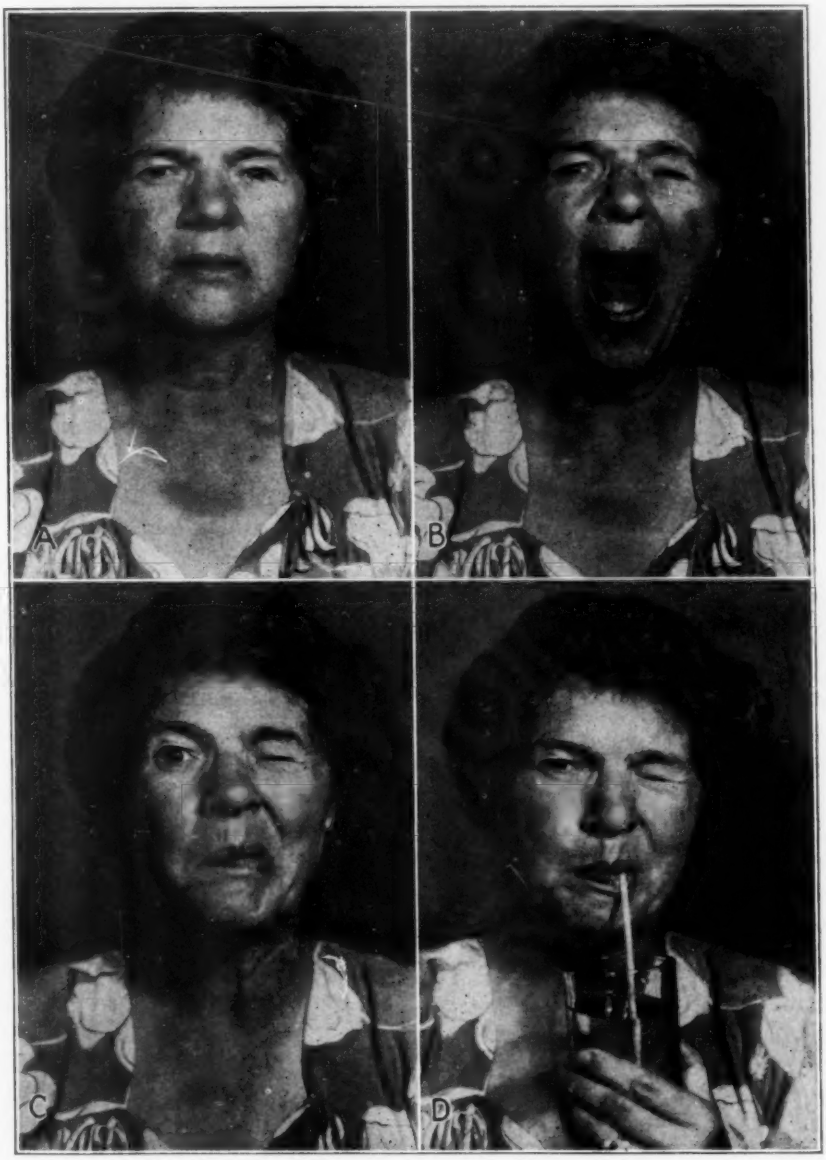

Fig. 4 (case 3).—Old left-sided peripheral facial palsy. *A*, face at rest; *B*, closure of the left eye on forceful wide opening of the mouth; *C*, closure of the left eye on moving the mouth to the left; *D*, closure of the left eye when patient sucks with the lips without movement of the mandible.

no associated movements from the trigeminal to the facial muscles here: there was no closure of the eyes when, for instance, the patient tightly squeezed a tongue blade between his teeth.

CASE 3 (fig. 4).—A 56 year old woman had Bell's palsy of the left side of the face five years ago. The recovery has been partial, and on the left side there is weakness of the facial muscles with mild contractures and associated movements. Figure 4, *A*, shows the face of the patient at rest. There is closure of the left eye on forcible wide opening of the mouth (fig. 4, *B*). A strong and complete closure of the left eye occurs when the patient is asked to move the mouth to the left (fig. 4, *C*). The left eye closes automatically when the patient is asked to suck through a straw placed between the lips, without movement of the mandible (fig. 4, *D*).

This series of illustrations demonstrate unequivocally the high susceptibility of the orbicularis oculi muscle to contract simultaneously on even the slightest provocation from other facial muscles when associated movements exist among them.

SUMMARY AND CONCLUSIONS

A motor phenomenon consisting in automatic closure of one eye on wide opening of the mouth has been described by German, Polish, Spanish, Belgian, French and Palestinian ophthalmologists and neurologists and has found its way into textbooks as well. It has been regarded as "unique," "paradoxical," "amazing," etc. It has been called "inverted Marcus Gunn phenomenon," and given the eponym "Marin Amat syndrome." It has been explained as an associated movement between the trigeminus and facial muscles, and this because the opening of the mouth was regarded as the primary mover. The critical analysis of the cases which present this phenomenon as described in the literature show that it occurred after peripheral facial palsy in which there was a tendency toward associated movements. It is thus evident that the so-called Marin Amat syndrome is nothing else but an intrafacial associated movement which commonly occurs after facial paralysis. The closure of the eye is contingent on movement of the lower facial muscles and not of the mandible. This closure of the eye is the commonest of all the associated movements among the facial muscles. The concept of Marin Amat syndrome as an inverted Marcus Gunn phenomenon and as a trigeminofacial associated movement does not stand up under critical analysis, and the whole syndrome, based on misconception, has no right to exist.

EXTERNAL OCULAR MUSCLE PALSIES OCCURRING IN DIABETES MELLITUS

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THE NEUROLOGIC complications of diabetes mellitus have been the subject of a number of reports in recent years. These have emphasized peripheral neuropathy and have related the pathogenesis mainly to metabolic disorder or to nutritional or vitamin deficiency. There is, however, growing evidence that vascular damage is an important factor. One of us (H. D.[1]) noted retinal hemorrhages in 200 patients with diabetes of up to twenty-five years' duration, while other forms of vascular disease, such as hypertension and/or albuminuria, were present in half of the group. The central nervous system does not escape in this generalized process. The classic syndrome of occlusion of the posterior inferior cerebellar artery occurs characteristically in diabetes, and pupillary abnormalities are common manifestations. This report describes the ocular palsies seen in 14 diabetic patients, all of whom showed evidence of vascular damage.

REPORT OF CASES

CASE 1.—*Homolateral oculomotor nerve palsy with reverse lid closure phenomenon in the contralateral eye and bilateral paralysis of pupillary accommodadation; previous palsy of the abducens nerve.*

S. G., a 32 year old housewife, was admitted to the hospital on Feb. 28, 1946, because of vertigo, diplopia and drooping of the left upper eyelid. She had been diabetic since the age of 10 and had had several admissions to hospitals during adolescence because of severe ketosis. She was maintained on 50 to 80 units of insulin daily, although glycosuria was never controlled without frequent hypoglycemia. In 1943 she had had an illness similar to the present one, when, after an infection of the upper respiratory tract, she complained of vertigo and diplopia. On examination, paralysis of the left external rectus muscle was found; the fundi showed many retinal hemorrhages and areas of degeneration, and the knee jerks and ankle jerks were depressed. At this time mild albuminuria and incipient

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1. Dolger, H.: A Clinical Evaluation of Vascular Damage in Diabetes Mellitus, Bull. New York Acad. Med. **22**:483, 1946.

hypertension were noted. The patient recovered completely from this episode and was well neurologically until three weeks before the present admission, at which time acute sinusitis developed. This was treated successfully with sulfathiazole. Ten days before her hospitalization, the patient's husband noticed that her left eye deviated outward, and five days later the patient complained of dizziness and diplopia. On the following day ptosis of the left eye and pain about the left leg developed.

On the examination on admission these conditions were observed: 1. There were hemorrhages and areas of degeneration in the retina with arteriosclerotic changes in the vessels. 2. The left upper eyelid was completely ptosed. With the aid of the compensatory action of the frontalis muscle, the lid could be raised slightly. Slight external strabismus was present in the left eye. 3. There was paralysis of internal rotation, upward movement and downward movement of the left eye. Good intorsion on the attempt to look downward indicated intact trochlear innervation. 4. There was miosis of the left pupil, which measured 1.5 mm. in diameter, whereas the diameter of the right pupil was 3 to 4 mm. Both pupils reacted well to light but did not react in accommodation. Convergence in the right eye was intact. 5. The ciliospinal reflex was intact bilaterally. 6. On elicitation of the lid closure phenomenon, there was no movement of the paralyzed left eyeball but the right eyeball rolled downward instead of upward. The pupil did not constrict and at times was seen to dilate. 7. The knee jerks and ankle jerks were noticeably diminished bilaterally. The spinal fluid was clear, was under normal pressure and contained no cells; the total protein content was 58 mg. per hundred cubic centimeters. A tourniquet test, application of 100 mm. of pressure over the upper arm, produced numerous petechiae within three minutes. The blood count, platelet count and bleeding, clotting and prothrombin times were normal. Roentgen examination of the skull revealed no abnormalities. Mild albuminuria and hypertension (systolic pressure 180 and diastolic 90) were observed. During the first few days of the patient's sojourn in the hospital, the miotic left pupil gradually became larger until ten days after admission it had a diameter 1 mm. greater than that of the right. Two weeks after admission, it was noticed that there had been improvement in the power of the left levator palpebrae superioris muscle and a slight nystagmus on left lateral gaze had appeared. One week later the lid closure phenomenon in the right eye had returned to normal, with rolling up of the eyeball and constriction of the pupil on forcible closure of the lids. Ten days later, further improvement in the left levator muscle was noted and a pseudo-Graefe phenomenon had appeared—i. e., elevation of the paretic lid when the patient looked to the right. Increase in the power of the left internal rectus muscle also was noted. The patient continued to improve, and eight weeks after onset it was observed that both pupils reacted partially in accommodation. Examination on May 6 showed almost complete return of function. The left pupil was larger than the right; accommodation had returned, and the lid closure phenomenon was intact bilaterally. There were still a pseudo-Graefe phenomenon and a slight rotatory binocular nystagmus on right lateral gaze, more pronounced in the abducted eye. Follow-up examination six months after onset showed the pseudo-Graefe phenomenon as the only abnormality in the cranial nerves except for the marked retinal damage.

CASE 2.—*Dissociated oculomotor nerve palsy.*

I. S., a 52 year old man, whose mild diabetes was controlled by diet alone for two years, was admitted to the hospital on Jan. 13, 1945. One week prior to

admission, supraorbital pain appeared on the right, and within the next two days the patient had noticed progressive diplopia and drooping of the right upper eyelid. Diabetes was discovered in 1943, when paralysis of the left side of the face appeared, which was diagnosed as Bell's palsy; it cleared in six weeks. At the time of his present admission, neurologic examination revealed no abnormalities except the dissociated paralysis of the muscles innervated by the left third cranial nerve. There were external strabismus and ptosis on the left. There was paralysis of internal rotation and upward movement in the left eye, but downward movement was only slightly limited. The pupillary actions were normal bilaterally. The ankle jerks were diminished, and vibratory sense was absent in the toes. Lumbar puncture yielded a clear fluid with an initial pressure of 170 mm. of water; the pressure after removal of 10 cc. was 110 mm. The total protein content was 52 mg. per hundred cubic centimeters. A roentgenogram of the skull showed normal conditions with a calcified pineal body in the midline. The electroencephalographic record was normal. The diabetes was easily controlled by diet and occasional small doses of insulin. The fasting blood sugar level was 151 mg. per hundred cubic centimeters; a trace of albumin was found, and the blood pressure was elevated to 150 mm. systolic and 100 mm. diastolic. The patient's condition gradually improved, and the neurologic abnormalities had completely cleared within six weeks after admission. Follow-up examination in April 1946 showed intact ocular movements. A single retinal hemorrhage was observed in the right eye.

CASE 3.—*Recurrent dissociated oculomotor nerve palsy.*

B. G., a 63 year old housewife, was admitted to the hospital on Dec. 24, 1946, because of headache and diplopia. Eight years previously she had had a similar episode of pain in the left eye and double vision, for which she had been treated at another hospital. Three weeks before the present admission, severe pain in the right orbit and nausea developed. The next day the pain had subsided, but the right upper lid was ptosed. When the lid was raised, double vision was present. Thereafter, headache had persisted intermittently. The ptosis had improved slightly, but diplopia continued. There was a history of diabetes of fifteen years' duration, for which the patient had received about 35 units of insulin daily. She had known of an elevation of blood pressure for about thirty years. Three years before admission, many retinal hemorrhages were noted bilaterally, in addition to a constant mild albuminuria.

On admission, the blood pressure was 190 systolic and 110 diastolic. Neurologic examination showed external strabismus in the right eye and ptosis of the same lid with paralysis of inward and upward rotation. There was only slight involvement of downward gaze. The pupils were equal and reacted well to light and in accommodation. In convergence the right eye came only as far as the midline, while the left reacted normally. Fundus examination showed many hemorrhages and old exudates, particularly in the right eye. The ankle jerks were absent, and vibratory sense was diminished in all toes. Lumbar puncture yielded clear fluid under an initial pressure of 180 mm. of water, which fell to 110 mm. after removal of 10 cc. of fluid. The fluid contained no cells; the total protein content was 65.5 mg. per hundred cubic centimeters. Under observation, the patient's condition gradually improved, and she was discharged six weeks after onset with only a slight ptosis. Subsequent examinations four weeks and four months later revealed no oculomotor abnormalities.

CASE 4.—*Oculomotor nerve palsy with intact pupillary function.*

P. S., a 57 year old woman with a ten year history of mild diabetes controlled by 10 units of protamine zinc insulin, was first seen neurologically in the outpatient department on Oct. 5, 1944. For the preceding two weeks, she had complained of headache, nausea, dizziness and pain in the right half of the face and behind the right ear. During this period she had also noticed drooping and inability to raise the right upper eyelid. Examination revealed right ptosis and paralysis of the right internal, superior and inferior rectus muscles. There was questionable hyperalgesia of the right half of the forehead. The pupillary reactions were normal. The fundi showed numerous retinal hemorrhages and exudates, and urinalysis revealed a faint trace of albumin. The blood pressure was 180 systolic and 95 diastolic. On October 12 the patient was noted to be improved, and seven weeks after the onset of her symptoms the ocular palsies had completely cleared.

CASE 5.—*Abducens nerve palsy.*

L. K., a 67 year old man, had been diabetic for fourteen years. The diabetes was controlled by diet alone for nine years, but 35 units of protamine zinc insulin had been required daily for the past five years. Hypertension (pressure 200 systolic and 100 diastolic), albuminuria and severe retinopathy had been noted for the past two years. On Oct. 11, 1945, he complained of double vision. Examination on the following day revealed paralysis of external rotation in the right eye. There were a severe retinopathy and corneal opacities. The patient gradually improved, and on November 15, the right eye could be rotated medially past the midline. Double vision persisted, however, until Jan. 2, 1946, two and one-half months after onset, when the ocular movements had returned to normal.

COMMENT

A striking feature of the neurologic manifestations in these cases is the lack of direct correlation with either the degree of severity of the diabetes or with the age of the patients. These factors had been generally assumed to play the main role in the development of vascular damage. Four patients had their diabetes well controlled by diet alone, requiring no insulin at any time. In 10 patients the diabetes was of mild to moderate severity, and only 2 patients presented a condition necessitating a large amount of insulin. Two patients in the fourth decade of life had had diabetes since childhood, with the onset at 10 and 14 years of age.

The one significant factor appeared to be the long duration of the diabetes. Ten patients had had the disease for from ten to twenty years. The shortest duration, two years, was noted in 2 middle-aged patients whose diabetes was so mild and asymptomatic that the onset of the disease must be indeterminate. Not infrequently the disease is manifested clinically with the development of a so-called "complication," such as retinopathy.

It has been stated that if a diabetic person lives long enough one or another form of vascular disease will develop.[2] Insulin, more adequate

2. Mirsky, I. A.: Our Challenge for the Future, Diabetes Abstr. **5**:71, 1946.

diets and improved measures for combating infection have preserved the lives of many young persons with diabetes, in whom the development of vascular lesions can now be observed. With 1 exception, all the patients displayed retinal hemorrhages at the time that the ocular palsy occurred. This patient showed a typical retinopathy with hemorrhages when examined fourteen months later. All the patients presented other evidences of vascular degeneration in the form of varying degrees of hypertension or mild albuminuria. Thus the ocular palsy represents but one manifestation of generalized vascular damage.

In 7 patients functions of the third nerve were affected. In 6, the sixth nerve was involved, while 1 patient had a combined third and sixth nerve palsy. All except 1 had clearing within three months' time. Two of the 14 patients had had previous ocular palsies. The onset was rapid, usually with diplopia and severe homolateral temporal or orbital pain. The neurologic signs pointed to the diagnosis of an intramedullary lesion of the brain stem rather than of a neuropathy affecting the nerve in its peripheral course. This conclusion was based on the presence of dissociated involvement in the cases with third nerve dysfunction and the disturbance of certain associated ocular movements in the contralateral, otherwise unaffected, eye.

Dissociation was present in 6 of the 7 patients with paralysis of the muscles innervated by the oculomotor nerve. In 3 of these there was paralysis of the levator palpebrae superioris and the superior and internal rectus muscles with sparing of the sphincter pupillae and the inferior rectus muscles. In 2 patients, all the extraocular muscles were involved and the reaction of the pupil in accommodation was lost while the reaction to light was preserved. In 1 patient there was only external ophthalmoplegia with intact pupillary function. One patient had only paralysis of the superior rectus muscle. Such dissociation occurs with lesions in the substance of the midbrain involving the oculomotor nucleus or the rootlets which emerge from it to form the peripheral nerve trunk. These fibers are spread over a large area, and a lesion in this region would be particularly likely to give rise to a dissociated paralysis. The pattern of dissociation is in accord with the functional localization in the oculomotor complex as described by Bernheimer [3] and Bender and Weinstein.[4] These authors found that in the oculomotor nucleus actions of the sphincter pupillae and inferior rectus muscle were represented most dorsally and rostrally. More ventrally and caudally, in the order named, were the functions of the internal rectus, superior

3. Bernheimer, S.: Experimentelle Studien zur Kenntnis der Innervation der inneren und ausseren vom Oculomotorius versorgten Muskeln des Auges, Arch. f. Ophth. **43**:481, 1897.

4. Bender, M. B., and Weinstein, E. A.: Functional Representation in the Oculomotor and Trochlear Nuclei, Arch. Neurol. & Psychiat. **49**:98 (Jan.) 1943.

rectus and levator palpebrarum muscles. Thus the dissociation seen in 3 cases with sparing of pupillary function and downward movement can be explained by a single lesion in the ventrocaudal portion of the oculomotor nucleus or its emergent rootlets.

In 2 patients with oculomotor nerve paralysis a disturbance of associated movements or synkinesis in the opposite, otherwise unaffected, eye was noted. In each there was bilateral paralysis of pupillary action in accommodation and convergence with preservation of the reaction to light. Reversal of the lid closure phenomenon in the contralateral eye was also present. Accommodation is normally associated with convergence movements of the eyes with pupillary constriction when the gaze is fixed at a near point. The lid closure phenomenon is a normal synkinesis in which there is upward rotation of the eyeballs and constriction of the pupils on forced closure of the lids. It is particularly noticeable in a patient with peripheral facial paralysis when an attempt is made to close the eye on the affected side. Stimulation of none of the cranial nerves produces this response; hence it is not a simple reflex. Weinstein and Bender [5] have shown that the phenomenon can be elicited by stimulation of the reticular substance in the region of the rubro-reticulo-olivary tracts in the midbrain and pons. The response is bilateral, even when only one side is stimulated. Like the mechanism of accommodation and convergence, the lid closure synkinesis is a pattern of cranial nerve function integrated within the substance of the brain stem. Its impairment and reversal on the side opposite to the extraocular palsy indicated that the causative lesion is in the tegmentum of the brain stem and not in the peripheral nerve trunk.

The description of ocular palsies in diabetes mellitus is not a recent development. In 1905 Dieulafoy [6] summarized the literature and reported 59 cases, including 1 of his own. He noted that the paralysis disappeared spontaneously in two to three months, that recurrences were not infrequent and that there was no relation between the paralysis and the severity of the diabetes. Leopold,[7] in a series of 100 cases of diabetes studied for ten or more years, noted a 5 per cent incidence of ocular palsy. Collier [8] studied over 30 cases and remarked that the ocular palsy often preceded the discovery of glycosuria. He noted dissociation in 2 patients and did not comment on any disturbance of

5. Weinstein, E. A., and Bender, M. B.: Integrated Facial Patterns Elicited by Stimulation of the Brain Stem, Arch. Neurol. & Psychiat. **50**:35 (July) 1943.

6. Dieulafoy, P.: Paralysie des nerfs moteurs de l'oeil chez les diabétiques, Presse méd. **13**:713, 1905.

7. Leopold, I. H.: Diabetes Mellitus as Observed in 100 Cases for 10 or More Years: Ocular Findings, Am. J. M. Sc. **209**:16, 1945.

8. Collier, J.: Paralyses of Oculomotor Nerve Trunks in Diabetes, Proc. Roy. Soc. Med. **23**:627, 1929.

associated ocular movements. He stated the belief that the cause was either a hemorrhage into the nerve trunk or a vascular lesion of the central nervous system on the basis of the diabetes. There was no opportunity for anatomic study in our patients, but, because of the rapid onset, the subsequent recovery, the evidences of vascular damage elsewhere and the constant observation of retinal hemorrhages, it is probable that the cause of the paralysis is an intramedullary hemorrhage. It is not necessary to postulate a "toxic neuritis" or a vague metabolic error when there is such extensive vascular disease. Treatment directed either at the underlying diabetes or at the neurologic complication was of dubious value, especially since in most instances the lesion cleared up spontaneously. When spontaneous clearing did not occur, extensive hemorrhage probably made the process an irreversible one.

SUMMARY

Fourteen cases of external ocular palsies in patients with diabetes are described. Seven patients had involvement of third nerve function; 6 had paralysis of sixth nerve action, and 1 had a combined oculomotor and abducens palsy.

The patients with third nerve palsies showed varying degrees of dissociation. In 2 there was a reversal of the lid closure phenomenon and a paralysis of pupillary action on convergence in the contralateral, otherwise unaffected, eye.

All the patients showed evidence of generalized vascular damage, with retinal hemorrhages in each. The neurologic lesion is not related to the age of the patient or the severity of the diabetes but is related rather to the duration of the disease.

GLIOBLASTOMA OF OCCIPITAL LOBE SIMULATING PSYCHOSIS WITH CEREBRAL ARTERIOSCLEROSIS IN AN OCTOGENARIAN

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THE increasing longevity of the state hospital population favors the occurrence of diseases hitherto rarely observed in very advanced age. Thus glioblastoma multiforme, commonest in the fifth and sixth decades of life, is hardly suspected in the ninth decade, when senile and vascular changes constitute the dominant pathologic alteration in the brain. The following case of a glioblastoma in an 81 year old man diagnosed as psychosis with cerebral arteriosclerosis illustrates this point and is of interest also because of the uncommon localization of the tumor in the occipital lobe.

REPORT OF A CASE

H. W. E., an 81 year old white farmer, had always been in good health with the exception of deafness and loss of vision of the right eye about one year prior to admission. His illness began about three months before entry to the hospital with the sudden development of weakness of the right hand, which progressed to a right-sided hemiplegia one month later. He also showed loss of memory and confusion as evidenced by failure to recognize his surroundings and by calling for his dead friends and parents. He was generally depressed and lethargic but, at times, restless and became excited, especially at night. Because of difficulty of caring for him at home he was transferred to the Taunton State Hospital.

On examination the patient was found to be a poorly nourished, drowsy and deeply confused old man with right hemiplegia. There was complete loss of memory for recent and past events; all thinking capacity was impaired, and little emotional reaction was elicited. The speech was feeble but normal otherwise. The pulse was regular, the blood pressure 140 systolic and 90 diastolic and thoracic and abdominal organs normal. There were bilateral cataracts with marked impairment of vision. The pupils were round and equal and reacted to light and in accommodation. The other cranial nerves appeared intact with the exception of a marked deafness. The tendon reflexes were hyperactive and Babinski's reflex was positive on the right side, but ankle clonus was not elicited. There was incontinence of urine and feces. The urine was acid; the specific gravity was 1.018 and chemical and microscopic changes were within normal limits. The blood count showed a hemoglobin content of 104 per cent, a red cell count of 5,200,000 and a white cell count of 8,600, with 68 per cent polymorphonuclear cells, 4 per cent stab cells, 27 per cent lymphocytes and 1 per cent monocytes.

From the Department of Pathology, Taunton (Mass.) State Hospital.

A diagnosis of psychosis with cerebral arteriosclerosis was made. The course remained unchanged, and the patient died eighteen days after admission to the hospital. Necropsy was done sixteen hours after death.

Postmortem Observations.—Gross: The brain with meninges weighed 1,480 Gm. before and 1,600 Gm. after fixation in formaldehyde solution U. S. P. The dura adhered firmly to the calvaria, and the arachnoid was fibrosed at the vertex of the hemispheres. The cerebrospinal fluid was decreased in amount and slightly xanthochromic, with a total protein content of 58 mg. per hundred cubic centimeters. The arteries of the circle of Willis and the cerebral hemispheres showed a moderate degree of arteriosclerosis. The left hemisphere was larger than the right; the convolutions were flattened, and the cerebellum showed a pressure cone. The left occipital pole was softened, especially at the inferior

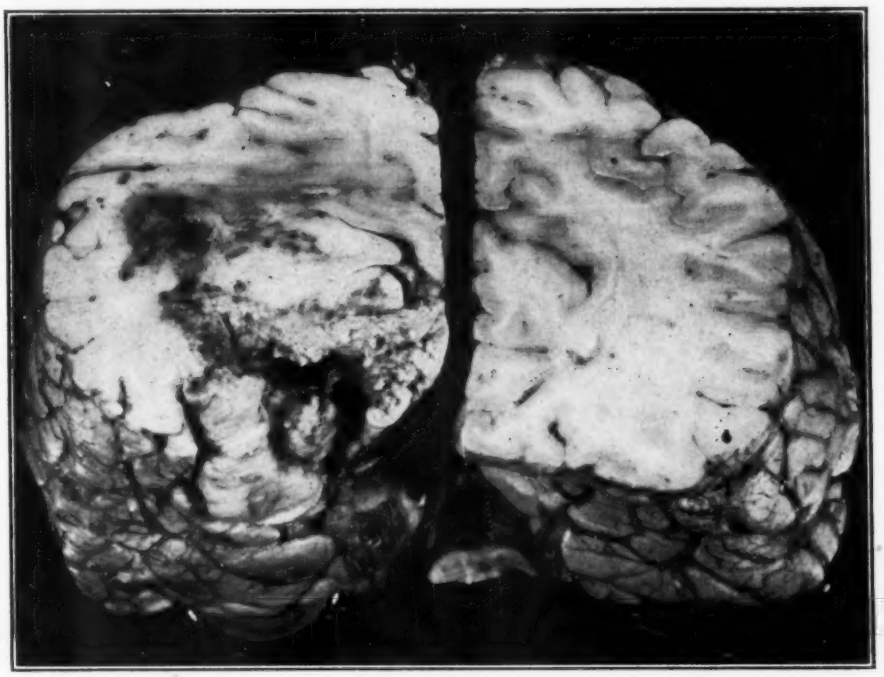

Fig. 1.—Glioblastoma of the left occipital lobe involving mainly the inferior and lateral portions, with large necrotic and hemorrhagic areas, some of which show green coloration.

surface. Coronal sections through the hemispheres revealed a large tumor in the left occipital lobe below and lateral to the posterior horn of the left lateral ventricle extending forward up to a plane through the posterior commissure (fig. 1). The tumor in anterior-posterior direction measured 11.5 cm. and on cross section up to 5 cm. in greatest dimension. No involvement of the motor, sensory or speech areas was noted.

The tumor tissue was soft and of mottled pink, tan and brown coloration interspersed with green zones.[1] There was extensive necrosis, especially in the

1. A similar green discoloration was observed by Adams in his case 2 (table 4). It may be explained as due to biliverdin which probably was formed by the action of formaldehyde on bilirubin present in old hemorrhagic extravasations.

posterior portions, and the left calcarine fissure was completely destroyed. In some places the tumor was well demarcated; in others the transition into the surrounding brain tissue was indistinct. The entire left hemisphere was markedly edematous and swollen, displacing all structures to the right, and the left cingulate gyrus was herniated underneath the falx. The posterior horn of the left lateral ventricle was completely obliterated; the anterior and inferior horns and the third ventricle were partly compressed and displaced. The ependyma of both lateral ventricles was stained with blood. The foramens of Monroe and the aqueduct of Sylvius were patent. Sections through the right hemisphere, pons, cerebellum and medulla did not reveal any gross changes.

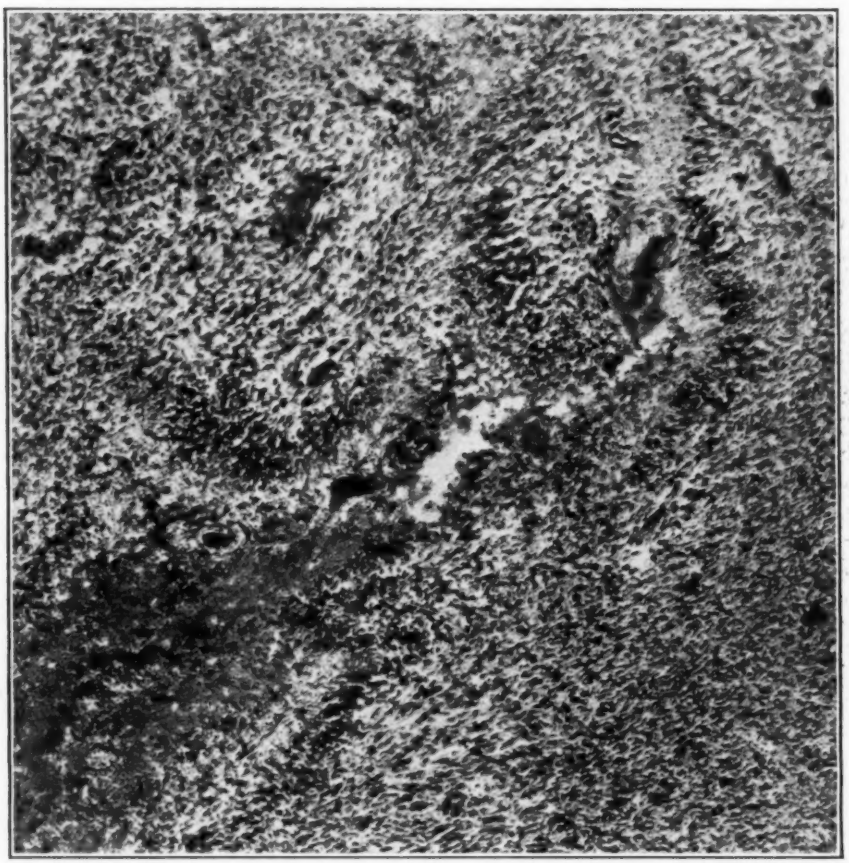

Fig. 2.—Photomicrograph of tumor area demonstrating pseudopalisading. Hematoxylin-phloxine stain; × 125.

The main conditions observed in the internal organs included bronchopneumonia of the lower lobes of both lungs, moderate aortic and valvular arteriosclerosis and nephrosclerosis.

Microscopic: In microscopic sections the tumor was found to be composed predominantly of small cells with elongated nuclei and scanty cytoplasm, varying in size and shape and arranged in irregular patterns. There were many cellular fields with sheets of cells, other relatively acellular fields and large areas of hemorrhage and necrosis. Pseudopalisading of cells around such hemorrhagic and necrotic areas was conspicuous (fig. 2). Scattered throughout the tumor

were many small and large multinucleated giant cells and also numerous mitotic figures. The tumor was very vascular, and some vessels exhibited adventitial proliferation and hyaline degeneration of the walls. Sections stained with Mallory's phosphotungstic acid hematoxylin and by Bielschowsky's silver method showed many cells with bipolar fibrillary processes. In sections from portions of the brain adjacent to the tumor there was evidence of degeneration of ganglion cells. Silver preparations of sections from the frontal poles showed some senile plaques.

COMMENT

Brain tumors in the aged have been studied by Moersch, Craig and Kernohan [2] whose 100 patients ranged in age from 60 to 84 years and who had various types of tumors. In Badt's [3] series of 57 undiagnosed brain tumors there were 2 meningiomas, 1 adenoma and 1 hemangioma but no glioblastoma in patients in the age bracket from 80 to 89 years. Data from the literature [4] compiled in table 1 show no cases of glioblastoma occurring in the ninth decade of life and only 2 in the eighth

TABLE 1.—*Age Incidence in 175 Published Cases of Glioblastoma*

Age Groups, Yr.	Source		
	Bailey and Cushing [4a] (77 Cases)	Elvidge, Penfield and Cone [4b] (56 Cases)	Single Cases Reported Since 1928 (42 Cases)
1-9	0	3	1
10-19	4	5	2
20-29	11	2	4
30-39	15	12	7
40-49	27	13	18
50-59	14	17	4
60-69	6	1	5
70-79	0	1	1
80-89	0	0	0

decade. A possible exception is a case quoted by Courville [5] and originally reported by Edes [6] in 1871 as an instance of multiple gliosarcoma in an 83 year old woman. Another case, also in an 83 year old woman, was observed by Adams [7] at the Boston City Hospital, and

2. Moersch, F. P.; Craig, W. McK., and Kernohan, J. W.: Tumors of the Brain in Aged Persons, Arch. Neurol. & Psychiat. **45**:235 (Feb.) 1941.

3. Badt, B.: Bericht über 57 nicht diagnostizierte Hirntumoren, zugleich ein Beitrag zur Symptomatologie der Hirntumoren im Senium, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:610, 1932.

4. (*a*) Bailey, P., and Cushing, H.: A Classification of Tumors of the Glioma Group on a Histologic Basis, Philadelphia, J. B. Lippincott Company, 1926. (*b*) Elvidge, A.; Penfield, W., and Cone, W.: The Gliomas of the Central Nervous System: A Study of Two Hundred and Ten Verified Cases, A. Research Nerv. & Ment. Dis., Proc. **16**:107, 1937.

5. Courville, C. B.: Multiple Primary Tumors of the Brain: Review of the Literature and Report of Twenty-One Cases, Am. J. Cancer **26**:703, 1936.

6. Edes, R. T.: Morbid Growths Connected with the Nervous System: Cerebrum, Cerebellum and Semilunar Ganglion of the Sympathetic, Am. J. M. Sc. **61**:87, 1871.

7. Adams, R. D.: Personal communication to the author.

the clinical diagnosis of glioblastoma of the left frontal lobe on the basis of electroencephalographic tracings was confirmed at autopsy.

Several authors [8] have studied brain tumors in psychotic patients (table 2) and the consensus seems to be that there is no significant difference when compared with similar age groups of nonpsychotic patients. However, a comparison of the principal intracranial tumors in patients in mental disease hospitals with those in general hospitals and neurosurgical patients shows marked differences. Such contrasting figures as are given in table 2 reveal that gliomas are about one and a half times less frequent in mental than in general hospital and neurosurgical patients, whereas meningiomas are about four and two times as frequent in patients with mental disease as in general hospital and neurosurgical patients respectively. From these figures it appears that meningiomas are the prevalent tumors in the old age group of psychotic patients, while gliomas—consisting mainly of glioblastomas—range sec-

TABLE 2.—*Incidence of Principal Intracranial Tumors in Autopsy and in Neurosurgical Material*

	Source Autopsy Material		
	State Hospitals [8a] (240 Brain Tumors from 6,958 Autopsies)*	General Hospital [8b] (188 Brain Tumors from 10,592 Autopsies)	Neurosurgical Material [8c] (4,532 Cases)
Gliomas	30.0†	43.1†	48.3†
Meningiomas	37.5	9.6	15.1
Pituitary adenomas	7.5	3.2	11.1
Metastases	11.7	15.4	3.7
Other tumors	13.3	28.7	21.8

* Including 21 brain tumors from 1,318 autopsies at the Taunton State Hospital.

† Figures give per cent of total brain tumors of each series.

8. (*a*) Blackburn, I. W.: Intracranial Tumors Among the Insane, Washington, D. C., Government Printing Office, 1903. Davidoff, L. M., and Ferraro, A.: Intracranial Tumors Among Mental Hospital Patients, Am. J. Psychiat. **8**:599, 1929. Hoffman, J. L.: Intracranial Neoplasms: Their Incidence and Mental Manifestations, Psychiatric Quart. **11**:561, 1937. Larson, C. P.: Intracranial Tumors in Mental Hospital Patients: A Statistical Study, Am. J. Psychiat. **97**:49, 1940. Zfass, I. S., and Riese, W.: A Preliminary Report of the Study of Two Hundred Autopsy Cases at the Eastern State Hospital with Special Emphasis on Neuropathology and Brain Tumors in Old Age, Virginia M. Monthly **71**:281, 1944. Crumpacker, E. L., and Riese, W.: Brain Tumors in State Hospital Patients: A Study of Eight Cases in One Hundred and Twenty Consecutive Autopsies, ibid. **72**:407, 1945. (*b*) Peers, J. H.: The Occurrence of Tumors of the Central Nervous System in Routine Autopsies, Am. J. Path. **12**:911, 1936. (*c*) Cushing H.: Intracranial Tumors, Springfield, Ill., Charles C Thomas, Publisher, 1932. Elsberg, C. A.: Some Facts Concerning Tumors of the Brain, Bull. New York Acad. Med. **9**:1, 1933. Olivecrona, H.: Die chirurgische Behandlung der Gehirngeschwülste, Berlin, Julius Springer, 1927. Toennis, W.: Ueber Hirntumoren, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:114, 1938.

ond in frequency and although rare in absolute figures cannot be discounted even in the ninth decade of life.

Another unusual feature of the present case is the localization of the tumor in the occipital lobe, whereas the favorite sites of glioblastomas are, according to Pette,[9] the anterior or middle portions of the hemispheres. The survey [10] in table 3 shows that a primary localization of glioblastomas in the occipital lobe, as distinguished from secondary extension of tumors in the parietal or temporal lobes, is almost as uncommon as that in the cerebellum or cord. Courville [5] has pointed out that multicentric glioblastomas are not uncommon, and among 134 cases he listed 22 in which the occipital lobe was the site of one of two or more primary tumors in the brain. However, a primary massive involvement of the occipital lobe is rare, and, with the exception of some instances not described in detail such as the occipital glioblastoma illustrated in Cushing's monograph (his figure 19), only 4 cases were collected from the literature (table 4).[11]

TABLE 3.—*Localization in 259 Published Cases of Glioblastoma**

	Kroll [10a]	Rowe [10b]	Toennis [8c]	Cases from Literature Since 1928
Total number	42	67	88	62
Per cent of total localized in				
Frontal lobe	16.7	18.5	21.6	27.4
Temporal lobe	42.8	35.3	22.8	21.0
Parietal lobe	7.2	20.0	14.8	19.4
Diencephalon	19.0	20.0	0	6.5
Brain stem	14.3	4.8	10.0	9.7
Occipital lobe	0	1.5	4.6	3.2
Cerebellum	0	0	0	3.2
Cord	0	0	0	3.2
Diffuse, central, septum pellucidum	0	0	26.2	6.5

* If multiple, the main localization only is considered.

As noted from table 4, the left occipital lobe was involved in 3 cases, and in all 4 cases there were similar gross changes and only minor variations in the microscopic pattern. In view of this fairly uniform pathologic picture, the heterogeneous clinical features, such as pituitary syndrome, visual hallucinations and hemiplegia, are noteworthy. Homonymous hemianopsia was observed in 2 cases, and headache and changes in eyegrounds and pupils were present in 3 cases. In all 4 cases there were some abnormalities of reflexes and mental changes, such as confusion and disorientation. Other psychiatric signs

9. Pette, H.: Klinik der Hirngeschwülste, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:10, 1938.

10. (*a*) Kroll, F. W.: Operative Erfahrungen bei Hirntumoren, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:188, 1938. (*b*) Rowe, S. N.: Glioblastoma Multiforme: A Study of Sixty-Five Cases, Tr. Am. Neurol. A. **61**:87, 1935.

11. (*a*) Balado, M., and Bernasconi Cramer, E.: Espongioblastoma multiforme del lóbulo occipital izquierdo, Arch. argent. de neurol. **2**:242, 1928. (*b*) Paulian, D., and Bistriceanu, I.: Contribution à l'étude histopathologique des glioblastomes névraxiaux multiformes, Ann. de méd. **37**:359, 1935.

TABLE 4.—*Summary of Reported Cases of Massive Glioblastomas of Occipital Lobe*

Author	Age, Sex	Pathologic Observations		Clinical Data			
		Gross	Microscopic	General	Neurologic	Psychiatric	Course
Balado and Bernasconi Cramer,[11a] 1928	34 ♂	Tumor of left occipital lobe; displacement; tumor variegated	Piriform and giant cells; rosettes; vascular proliferation; hemorrhage, necrosis	Pituitary syndrome; polyuria; female habitus; headache; vomiting; poor vision	Left papilledema; right homonymous hemianopsia	Confusion; childish behavior; anxiety	Operations; duration 6 mo.
Paulian and Bistriceanu,[11b] case 2, 1935	66 ♂	Tumor of left occipital and parietal lobes; compression of left lateral ventricle	Irregular cells around vessels; vascular proliferation; some calcification	Sudden onset with loss of consciousness; headache	Right pupil larger than left; impaired hearing; reflexes on left stronger than on right	Disorientation; memory defect; speech disturbances	Right hemiplegia; duration 7 mo.
Adams,[7] case 2, 1945	63 ♀	Tumor of right occipital lobe; surface flattened; herniation; tumor variegated, partly green	Variation in shape; delicate fibers; no giant cells; hemorrhage; necrosis	Headache; vomiting; loss of consciousness; pain in eyes; poor vision	Pupils fixed; left papilledema; left homonymous hemianopsia; facial weakness; diminished reflexes in left leg	Confusion; disorientation; visual hallucinations	Drowsiness; infection after operation; duration 5 mo.
Naumann	81 ♂	Tumor of left occipital lobe; edema; displacement; herniation; tumor variegated, partly green	Variation in size and shape; fibrillary processes; giant cells; pseudopalisading; hemorrhage, necrosis	Sudden onset with paresis of right hand; right hemiplegia; deafness; cataracts	Pupils reacting; reflexes hyperactive on right; Babinski sign on right; incontinence	Confusion; memory defect; restless at night; depression	Duration 3½ mo.

varied from childish behavior and anxiety to restlessness and depression, memory defects and visual hallucinations. Such hallucinations, present in Adam's case, are the only localizing sign pointing to the optic center and conforms to Unsworth's [12] statement that visual as well as auditory hallucinations may be found in the occipital lobe growths. Visual agnosia was not observed in any case, but allowance must be made for the difficulty of making such observations in confused patients. That unilateral lesions of Brodmann's areas 17, 18 and 19 may not necessarily cause agnosia has been demonstrated by Nielsen [13] and was shown in a drastic way by Foerster, who removed an entire left occipital lobe, seat of an oligodendroglioma, as reported by Lange and Wagner.[14]

Several writers [15] have described the frequent sudden onset of symptoms in glioblastomas which may be mistaken for a vascular accident, especially in the presence of hemiplegia. If these findings are coupled with memory defect and mental changes in an old person, and if, in addition, examination of the eyegrounds and visual fields is prevented by cataracts, as in my case, a diagnosis of psychosis with cerebral arteriosclerosis may in some instances be unavoidable. A helpful differential sign pointed out by Caron [16] may be the fluctuating character of a paralysis in brain tumors due to the changing state of the concomitant cerebral edema.

SUMMARY

A case of glioblastoma multiforme of the left occipital lobe in an 81 year old man with the clinical picture of psychosis with cerebral arteriosclerosis is presented. The age of incidence, localization and some clinical aspects of gliomas in elderly psychotic patients are discussed.

Raymond D. Adams, assistant professor of neurology, Harvard Medical School, permitted me the use of his records in this investigation.

12. Unsworth, H. R.: Psychiatric Aspects of Cerebral Tumors, New Orleans M. & S. J. **95**:363, 1943.

13. Nielsen, J. M.: Agnosia, Apraxia, Aphasia: Their Value in Cerebral Localization, New York, Paul B. Hoeber, Inc., 1946.

14. Lange, H., and Wagner, W.: Kompensationsschritte bei Zerstörung des linken Occiptallappens durch einen Tumor, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:199, 1938.

15. Locke, C. E.: The Differential Diagnosis of Brain Tumors, Ann. Clin. Med. **5**:1097, 1927. Elsberg, C., and Globus, J. H.: Tumors of the Brain with Acute Onset and Rapidly Progressive Course: "Acute Brain Tumor," Arch. Neurol. & Psychiat. **21**:1044 (May) 1929. Globus, J. H., and Strauss, I.: Vascular Lesions and Tumors of the Brain: Difficulties in Differential Diagnosis; Report of Seven Cases with Necropsy Findings, ibid. **15**:568 (May) 1926. Stender, A.: Apoplektiformer Krankheitsbeginn bei Hirntumoren (Halbseitenlähmungen), Ztschr. f. d. ges. Neurol. u. Psychiat. **163**:123, 1938. Weisz, S.: Brain Tumor and Cerebral Vascular Disorders (Differential Diagnosis), Dis. Nerv. System **8**:23, 1947.

16. Caron, S.: Quelques considérations cliniques au sujet d'un gliome cérébral, Laval méd. **9**:768, 1944.

MASSIVE HEMORRHAGE IN BRAIN TUMORS

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A HISTORY of sudden onset of symptoms in cases of brain tumor is not uncommon. The usual explanation for the apoplectiform attack is that a vascular accident or gross hemorrhage occurred into the tumor. This theory, however, is not supported by clinicopathologic investigations.[1] In 1933 Oldberg [2] reviewed 832 consecutive cases of glioma of the brain. Gross hemorrhage was found in only 31, or 3.72 per cent, of the cases. In only 7 were there striking features of vascular accident, such as sudden onset or acute exacerbation of symptoms. It is evident, then, that in less than 1 per cent of cases of glioma of the brain is gross hemorrhage responsible for the abrupt onset of symptoms. Similar statistical data were obtained in other types of brain tumor. Although the incidence of hemorrhage into tumor is generally low, during the past year we have observed 4 such cases.

REPORT OF CASES

CASE 1.—V. M., a white woman aged 49, previously in good health, bumped her head on a cabinet door nine days before admission to the Mount Sinai Hospital. There was no loss of consciousness, and the injury was considered trivial. Two days later, however, she awoke with a severe headache. The headache persisted and became more intense. There was increasing drowsiness. When admitted to the hospital nine days after the accident, the patient was in stupor. The pulse rate was 60; the blood pressure was 118 systolic and 70 diastolic. The left pupil was larger than the right. There was a left hemiparesis. A diagnosis of subdural hematoma was made. Bilateral trephinization did not disclose a subdural hematoma. Lumbar puncture performed the next morning yielded a xanthochromic fluid containing 1,500 crenated red blood cells per cubic millimeter. A roentgenogram of the skull showed the pineal gland shifted to the left and backward. Craniotomy of the right frontal area showed the sylvian vessels displaced upward. The superior temporal convolution had a yellowish discoloration.

From the Neurosurgical and the Neurological Services of the Mount Sinai Hospital.

1. Globus, J. H., and Sapirstein, M.: Massive Hemorrhage into Brain Tumor, J. A. M. A. **120**:348 (Oct. 3) 1942.

2. Oldberg, E.: Hemorrhage into Gliomas, Arch. Neurol. & Psychiat. **30**:1061 (Nov.) 1933.

A transcortical incision disclosed a blood clot about 2 cm. in diameter 1 cm. below the cortex. When this was removed, it was evident that the hemorrhage had taken place within a large necrotic neoplasm. The patient improved temporarily but then relapsed and died three weeks later. At postmortem examination the right temporal lobe was seen to be larger than the left, and a mass 2.5 by 3 by 5 cm. was present in it (fig. 1). The microscopic diagnosis was hemangioendothelioma.

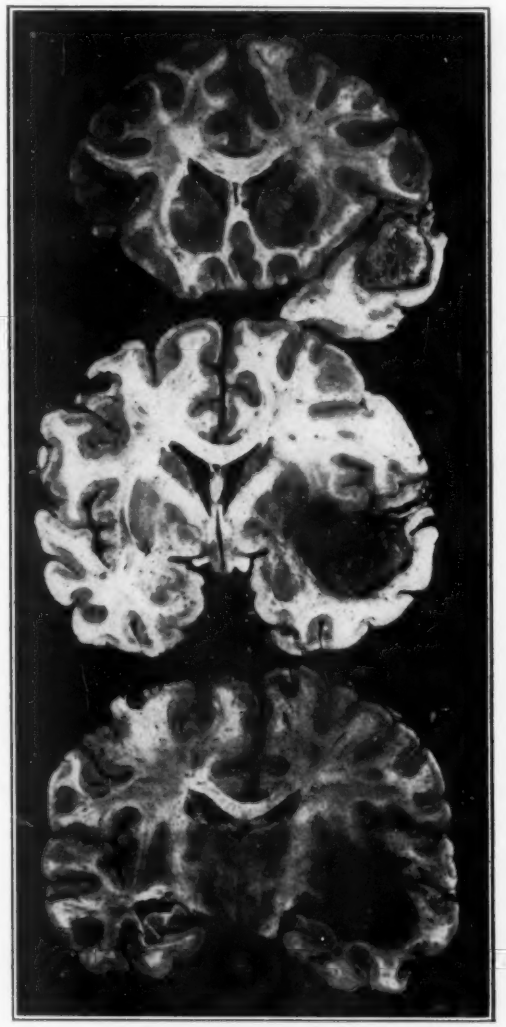

Fig. 1.—Hemorrhage into a hemangioendothelioma of the right temporal lobe.

CASE 2.—B. C., a white woman aged 53, fell down a few steps three and one-half weeks before admission to the Mount Sinai Hospital. She sustained minor injuries to her hip. There was no apparent head injury and no disturbance of consciousness. After this accident it was noted that the patient was unusually upset and anxious. Ten days before admission difficulty in speech and weakness in the right hand developed. Later there was difficulty in writing, and the patient began to drag her right leg. On admission the blood pressure was 140 systolic

and 70 diastolic. She was alert and cooperative. There was a right hemiparesis with concomitant pyramidal tract signs. The spinal fluid was xanthochromic and contained 2,160 red blood cells per cubic millimeter. The spinal fluid pressure was 100 mm. An electroencephalogram indicated the presence of a focus in the left inferior frontal and parietal areas. The paralysis and speech defect became more pronounced. There was no headache. The differential diagnosis rested

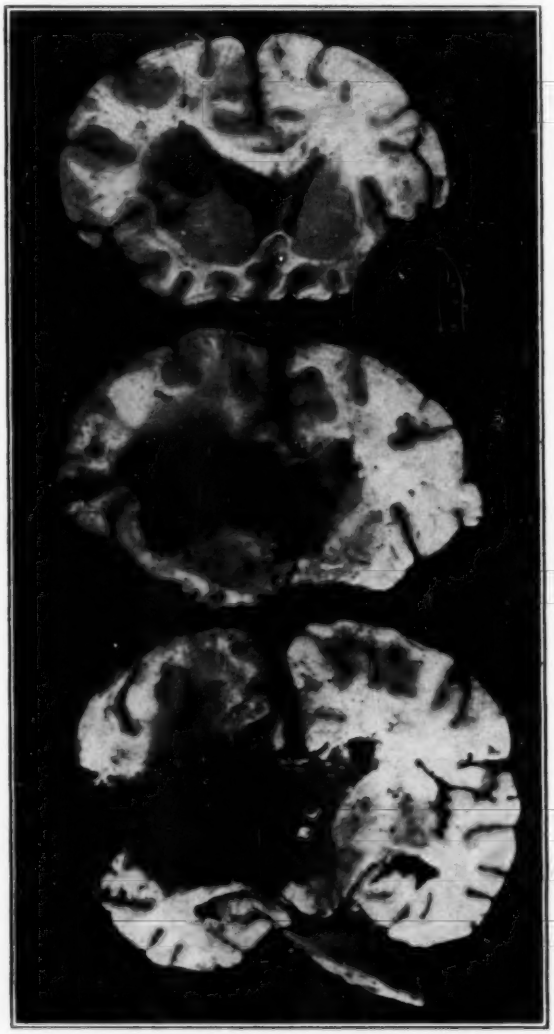

Fig. 2.—Disorganization and discoloration in the left cerebral hemisphere due to hemorrhage and transitional cell glioma.

between tumor and vascular lesion. The patient was prepared for pneumoencephalography, but fifteen minutes before it was to be carried out she became deeply comatose and spastic throughout her body. A trephine exploration disclosed an extensive intracerebral hematoma extending into the ventricle. The patient died twelve hours after the operation. Postmortem examination showed the left hemisphere to be larger than the right. In the left hemisphere, most prominent

at a point level with the mamillary bodies, there were extensive discoloration and disorganization due partly to hemorrhage and partly to tumor formation (fig. 2). The microscopic diagnosis was transitional cell glioma.

CASE 3.—H. C., a white woman aged 39, was admitted to Mount Sinai Hospital on Sept. 13, 1946. On August 26, she had tripped on the stairs and bruised her right shoulder. On August 30, there suddenly developed a severe pounding headache, nausea and vomiting. Two days later her left hand became weak and she complained of seeing flashes of light. On examination the patient was torpid; she had a left homonymous hemianopsia, left hemiplegia and left hemilateral

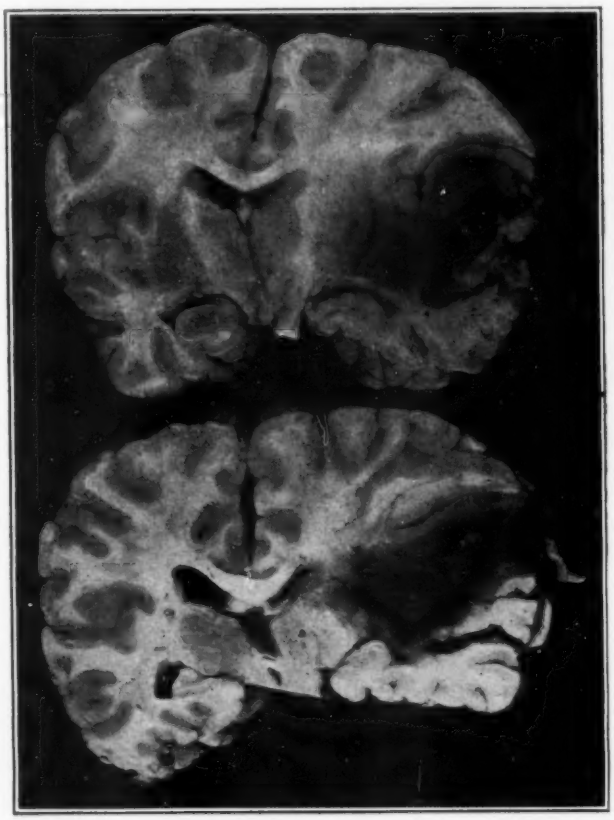

Fig. 3.—Metastasis in the right temporo-occipital region from a gastric carcinoma, with hemorrhage.

sensory disturbances with astereognosis in the left hand. The pulse rate was 65, and the blood pressure was 110 systolic and 70 diastolic. The spinal fluid was clear and colorless, contained 1 cell and was under a pressure of 144 mm. of water. The electroencephalogram indicated a focal lesion in the right temporo-parieto-occipital area close to the angular gyrus. On September 17, trephine exploration was done in the right occipital region, and 100 cc. of chocolate-colored fluid was removed from a cavity in the occipital lobe. The patient improved temporarily. The cavity was retapped on September 20. The symptoms fluctuated. On September 27, the patient became stuporous. On September 28, craniotomy of the right occipital-parietal region was done, and a large subcortical cystic cavity

was disclosed. The walls were wrinkled and covered with a velvety brown material about ⅛ inch (0.3 cm.) thick. The cavity extended forward to the posterior part of the temporal lobe. After the operation the patient improved greatly for a few days—in fact, to such an extent that she was able to walk. However, within two weeks the headache and vomiting recurred. The patient's condition declined, and she died on October 23. Postmortem examination showed a carcinoma of the stomach with numerous intra-abdominal metastases. There was a large metastasis in the right temporo-occipital region (fig. 3).

CASE 4.—B. G., a white woman, aged 68, was admitted to the hospital on Feb. 7, 1947. Her illness began in September 1946, when she complained of the sudden onset of severe right frontal headache. This was followed by bouts of vomiting and then loss of consciousness. The patient was kept in bed and after several weeks improved. Subsequently she resumed her household duties and seemed well until January 15, 1947, when the right-sided headaches recurred. At this time left hemiparesis was noted. The weakness in the left side of the body progressed; the patient became drowsy, and on the day of admission to the hospital she became stuporous. Examination on admission revealed left hemiplegia with concomitant pyramidal tract signs. The blood pressure was 130 systolic and 80 diastolic; the pulse rate was 120. Lumbar puncture yielded clear xanthochromic fluid under an initial pressure of 216 mg. of water. The fluid contained 1,630 crenated red blood cells. The rest of the laboratory data were normal. The patient's state of consciousness fluctuated from day to day. At one time she was alert, and at another she was stuporous. Ten days after admission bilateral trephinization was performed. Subdural clot was not found. Introduction of a needle into the right inferior parietal region disclosed a dark red plum-sized clot. This was situated about 3 cm. below the cortex. Postoperatively the patient improved. However, she soon became stuporous and died on March 7. Autopsy examination showed an infiltrating tumor the size of a lemon, extending from the region of the operative site into the occipital lobe on the right side. The microscopic diagnosis was spongioblastoma multiforme.

COMMENT

This is a small series of cases and sweeping conclusions cannot be drawn, but there are some features which are worth stressing. One is the symptomatology and second is the pathology. An analysis of the 4 cases fails to reveal a symptom complex which would be pathognomonic of hemorrhage into a brain tumor. It would seem that suddenness of onset should suggest a vascular accident of some sort. However, in only 2 of our 4 cases and 7 of Oldberg's 31 cases was there such suggestion. Moreover, one finds that sudden development of symptoms occurs not infrequenlty in cases of brain tumor without complicating hemorrhage. Other conditions which must be considered in the differential diagnosis of an acute onset of cerebral symptoms are "spontaneous" subarachnoid hemorrhage, massive cerebral hemorrhage, localized intracerebral hematoma, subdural hemorrhage and vascular or other malformation with hemorrhage. In our cases of hemorrhage in brain tumor the diagnosis was made either by surgical inspection or autopsy examination or both and not on clinical grounds.

When a hemorrhage within the brain is found at operation, one should not dismiss it as a case of intracerebral hematoma. Unless there is a history of trauma or unless there is evidence of vascular disease, the intracerebral hematoma should be suspected of being due to a neoplasm. This is especially true when the patient's symptoms are suggestive of tumor. All efforts should be directed toward establishment or exclusion of the presence of a neoplasm in the tissues surrounding the hemorrhagic cavity.

SUMMARY

Four cases of hemorrhage within brain tumor are reported.

There is no syndrome which is pathognomonic of hemorrhage into brain tumor.

When intracerebral hematoma is found at operation, it should be suspected of being due to brain tumor.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Diseases of the Spinal Cord

DEFORMITIES OF DURAL POUCHES AND STRICTURES OF DURAL SHEATHS IN THE CERVICAL REGION PRODUCING NERVE ROOT COMPRESSION. RAGNAR FRYKHOLM, J. Neurosurg. **5**:403 (Sept.) 1947.

In 7 cases of involvement of the cervical nerve roots in which operation was performed, Frykholm found that if the dural sheaths were opened the patients recovered rather promptly.

The signs and symptoms of a brachial neuralgia may, in some cases, be due to a thickening of the dural pouch, resulting in an acute angulation of the nerve root as it passes from its origin to the dural sheath. Concurrently, there may be stenosis of the intervertebral canal by a calcified herniation of an adjoining intervertebral disk. Removal of the disk alone will not effect a cure; but the extreme nerve angulation must be corrected by opening the dural sheath and relieving the constriction.

The author believes that the deep-seated shoulder girdle pain and muscular spasm is caused by compression of the motor root, while the radiating distal pain or numbness is due to involvement of the sensory root. A similar cause may be present in the lumbar region, and involvement of the sheath should be looked for in the 10 or 12 per cent of "negative explorations" performed at this level.

TOZER, Philadelphia.

POSTOPERATIVE SPINAL ADHESIVE ARACHNOIDITIS AND RECURRENT SPINAL CORD TUMOR. LEO M. DAVIDOFF, HARVEY GASS and JACOB GROSSMAN, J. Neurosurg. **5**:451 (Sept.) 1947.

Davidoff, Gass and Grossman report 5 cases of redevelopment of symptoms of compression of the cord after the removal of benign tumors of the spinal cord. The interval between the original operation and the recurrence of symptoms varied from three to fourteen years. In 1 case, there was a recurrence of the original tumor, while in the remaining 4 cases the symptoms were due to arachnoidal adhesions. On retrospective analysis, it was concluded that differential diagnosis of the two conditions was impossible, even with the use of myelography, and that exploration was indicated in all cases. At the time of operation thorough exploration should be made for a recurrent tumor, even if arachnoiditis is present. It is thought possible that recurrent tumor tissue may be the underlying cause of these adhesions. With the redevelopment and regrowth of the tumor, the surrounding dura undergoes hypertrophy and causes phenomena of compression.

The prognosis for patients with an arachnoiditis of this type is poor, even after reexploration.

TOZER, Philadelphia.

PROTRUSION OF INTERVERTEBRAL DISKS. R. H. YOUNG, Proc. Roy. Soc. Med. **40**:233 (March) 1947.

In a series of 248 patients with sciatica treated by methods other than laminectomy from 1939 to 1942, 79 per cent were still in pain or having attacks, and only

21 per cent were free from symptoms. Since 1942, 310 patients (all but 9 of whom had severe sciatica) have had laminectomies, and 80 per cent of these were symptom free in 1946. Of 533 patients on whom laminectomy was performed for sciatica and backache, lesions of the disk were found in 470 and spondylolisthesis in 20.

Of 45 patients with backache alone, all but 2 had a lesion of the disk. The earliest symptom in 470 cases of proved lesions of the disk was backache, in 68 per cent, followed by sciatica in 24 per cent.

In general, Young believes that pain in the lower part of the back without physical signs is due to visceral lesions or neurosis, and that pain with physical signs is due to a lesion of the disk unless the roentgenogram shows other conditions. With a history of recurrent backache and stiffness, and the sign of restricted forward bending with sidewise bending free and negative roentgenograms, the diagnosis can easily be made. Neurologic signs were present in only 40 per cent of proved cases. Sciatic scoliosis is always due to a lesion of the disk.

Operation was performed for only about half the conditions diagnosed as lesions of the disk. A trial of rest in bed for three weeks is given in first attacks, and if pain persists operation is recommended.

Although 95 per cent of the lesions are in the two lowest disks, the neurologic signs of changes in the ankle jerks and sensory changes are absent in 40 per cent of the cases and are absent in similar proportions with lesions of the disks between the fourth and fifth lumbar and the fifth lumbar and first sacral vertebrae; therefore, neurologic signs are useless in localization and are of value only in confirmation of the diagnosis. For this reason, the author operates with the patient on his side and removes the fifth lamina and adjacent ligamenta flava. In order not to miss the disk protrusion, operation is performed only during an attack. The lesion found at operation is either a protrusion of the nucleus pulposus or a tear in the annulus fibrosus.

In summary, the author states: "(1) Almost all sciatica and recurrent backache is due to disk lesions. (2) The diagnosis can be made on back signs alone. (3) Only operation offers the patient a definite prospect of cure." BERRY, Philadelphia.

VERTEBRAL HEMANGIOMA AND ITS NEUROLOGIC MANIFESTATIONS. E. KATZENSTEIN, Schweiz. Arch. f. Neurol. u. Psychiat. **58**:130, 1946.

Katzenstein reviews the literature and reports 3 cases of vertebral hemangioma. Examination of a man aged 56 revealed, in addition to signs indicative of advanced multiple sclerosis, marked tenderness on percussion over the spinous processes of the third and fourth thoracic vertebrae. Sensation was diminished in the corresponding segmental areas, which were bordered above and below by zones of hyperesthesia. Roentgenologic examination revealed advanced decalcification in the bodies of the third and fourth thoracic vertebrae, with structural alterations characteristic of hemangioma. Both diagnoses were confirmed by postmortem examination.

In the second case, that of a man aged 32 when first seen, pain between the shoulder blades was attributed to an attack of mild encephalitis with which the patient seemed to be suffering at the time. On reexamination thirteen years later, it was learned that the pain had persisted and that it had become severer after a recent fall; it was aggravated by coughing and sneezing, as well as by bending the spine. The spinous processes of the fourth, fifth and sixth thoracic vertebrae were tender on percussion. Thermhypesthesia and hyperesthesia for other qualities were noted in the fourth and fifth thoracic segmental zones. The original roentgenologic diagnosis of spondylitis deformans was changed to that of hemangioma when

further study revealed characteristic changes in the body of the fifth thoracic vertebra. After roentgen treatment, the pain was at first aggravated and later became less severe.

The third patient, a man aged 28, experienced increasing numbness in his lower limbs for several months before he complained of pain in the back with a girdle sensation and increasing unsteadiness in the legs. In addition to a spastic-ataxic gait, examination revealed a narrow band of hyperesthesia at the fifth thoracic level with diminished sensation below. The cell count and concentration of protein were considerably higher in two samples of cerebrospinal fluid obtained by lumbar puncture than in one removed from the cistern. The Queckenstedt test was evidently not done. The signs of a transverse lesion of the spinal cord became more pronounced, and a myelograph disclosed a complete block at a level between the bodies of the fourth and fifth thoracic vertebrae. Changes in the body of the fifth thoracic vertebra noted in the roentgenograms were thought to be characteristic of hemangioma. There was profuse bleeding during laminectomy, but subsequent examination of the bony fragments which were removed did not show any evidence of hemangioma. Although the spinal cord did not appear to be compressed, the patient gradually improved after operation, which was followed by roentgen treatment, and was able to return to work seven months later.

DANIELS, Denver.

Treatment, Neurosurgery

DISCUSSION ON LEUCOTOMY AS AN INSTRUMENT OF RESEARCH. Proc. Roy. Soc. Med. **40**:141 (Feb.) 1947.

Neuropathologic Studies. A. MEYER and T. MCLARDY.

In a series of 27 cases, Meyer and McLardy present a table demonstrating the variability of the lesions produced in prefrontal leukotomy; in only a few cases was the ideal lesion, i. e., a bilateral lesion through the whole of the white matter, obtained. The organization of the thalamofrontal projections (particularly of the dorsomedial nucleus), the frontopontile tract and the long association bundles received the major emphasis. In the clinicopathologic investigation, the reality of the personality changes and their possible substrate received primary attention. The problem was approached in the light of Sherrington's concept that the hypotheses of localized versus holistic function are not mutually exclusive but, on the contrary, are complementary. The localization in the frontal lobes of emotional and personality integration has met criticism from many sides, both phylogenetically and clinically. The point made by Hebb is emphasized, namely, that in all cases of bilateral pathologic involvement or surgical removal of the frontal lobes there is a possibility that the pathologic process itself, rather than the loss of frontal lobe tissue, may be responsible for the mental changes. A provisional analysis of the authors' cases reveals that 6 of 19 patients showed symptoms of a frontal lobe deficit, such as euphoria, facetiousness, apathy, lack of initiative or overactivity. There was no significant difference in the lesion between these 6 cases and the remaining cases. Considering the possibility that the position of the lesion may, as suggested by Dax and Radley-Smith, have specificity in alleviating certain symptom complexes, the authors state that "there may be a positive trend of correlation between improvement of depressive symptoms and orbital region involvement," but that as for the idea that a dorsal cut alleviates aggression and a middle cut, paranoid symptoms, no evidence of such a correlation has as yet been forthcoming. Bilateral involvement

of the medial segments of the prefrontal region (areas 24 and 32) in 3 cases was associated with prolonged confusion, as observed by Freeman and Watts, but no prognostic value is attributed by Meyer to this confusion. Involvement of the striatal region in 2 cases was associated with severe restlessness and in 1 case with rhythmic head movements. Vasomotor and trophic changes in the extremities resulted from bilateral involvement of area 6.

Electroencephalographic Studies. G. D. GREVILLE and S. L. LAST.

The electroencephalograms of 35 patients with various psychiatric disorders who had prefrontal leukotomies were examined before operation and at frequent periods up to one year after the procedure. The voltage of the alpha rhythm tended to increase after the operation, and the relative length of the record occupied by the alpha rhythm likewise increased. The voltage of the fast activity tended to decrease and there was indication that the amount tended to diminish after operation. More than half the patients at one time or another showed delta (less than 4 per second) activity, at first at random but later more paroxysmally. Delta activity was more pronounced during the first ten days after operation and appeared at first, perhaps, all over the cortex but soon predominated in the frontal region. Bipolar recording demonstrated that this activity originated in front of the cut. "There is some indication of a positive correlation between clinical improvement and the appearance of delta activity." Theta activity (4 to 7 per second) was found to be present in a higher percentage of cases than delta activity, and this percentage remained more constant with time, but while theta activity continued to appear in later records the amount in each record tended to diminish. No particular degree of correlation was noted between the degree of aggressive behavior and the theta activity. The hypothesis is advanced by the authors that the delta activity, commonly thought to arise from damaged gray matter or that functioning at a reduced level, is caused by the functional isolation of the prefrontal cortex from the rest of the brain, causing large groups of cells in the former to discharge synchronously.

Physiological Research in Progress. DR. F. REITMAN.

The changes in parasympathetic functions as evidenced by the study of the influence of the vagus nerve on gastric function were discussed. In the 9 cases studied the fibers from the orbital surface from areas 11 and 12 were thought to be severed. Statistically significant differences were found between preoperative and postoperative test meal curves: After leukotomy the total acidity was reached earlier, and the emptying time was shortened. The maximum change occurred five weeks after operation, and the curves ten weeks after leukotomy approximated the preoperative levels. It is suggested that the transient autonomic changes described may have a cortical (orbitofrontal), rather than an hypothalamic, basis.

Psychological Aspect. DR. M. B. BRODY.

Further evidence was presented that prefrontal leukotomy does not impair the capacity to perform mental tests, either intelligence tests or those of the Goldstein type. An interesting phenomenon was observed in some cases in that spontaneous ideation and activity did not reach the intellectual level and quality proved by the tests to be within the patient's capacity, a factor which the author correlates with the clinical observation that after leukotomy ideas formerly held with great emotion may remain unchanged, but stripped of that emotion, the fading of the emotion often preceding the fading of the ideas themselves.

BERRY, Philadelphia.

Experimental Pathology

LOW BACK PAIN ASSOCIATED WITH VARICES OF THE EPIDURAL VEINS SIMULATING HERNIATION OF THE NUCLEUS PULPOSUS. BARNARD S. EPSTEIN, Am. J. Roentgenol. **57**:736 (June) 1947.

Epstein reports 3 cases in which pain in the lower part of the back was due to varices of the epidural veins. Myelographic studies, made in 2 cases, disclosed a persistent filling defect in the column of pantopaque® (ethyl indophenylundecylate), and the diagnosis of herniated disk was made. The clinical diagnosis in the third case was also herniation of the disk.

In the 2 cases with lumbosacral defects in the column of oil, narrowing of the lumbosacral space was also apparent on conventional films.

Coughing, sneezing or straining, by producing dilatation of the veins, produced exacerbation of the clinical symptoms. Both the clinical and the roentgenographic signs are indistinguishable from those of herniation of the disk. Dilated pial veins give a roentgenologic appearance quite different from that of epidural varices. The pial veins are surrounded by the pantopaque,® producing channel-like, radiolucent shadows.

Surgical decompression was followed by relief in all 3 cases.

TEPLICK, Philadelphia.

Congenital Anomalies

A FAMILY WITH SPASTIC HEREDODEGENERATION. M. KLINGLER and W. BLOCH, Schweiz. Arch. f. Neurol. u. Psychiat. **58**:273, 1947.

In the genealogic table prepared by Klingler and Bloch, 242 persons, comprising nine generations, are listed. Beginning with the fifth generation, reliable information was, with few exceptions, obtained in regard to all members of the family. No instance of consanguineous marriage was discovered. Progressive spastic weakness of the lower limbs first appeared in a member of the sixth generation, a man born in 1849, whose symptoms became manifest when he was about 45. His 6 siblings and all their descendants were apparently free of the disease, as were all members of collateral lines. Of his 9 children, 5 had lived long enough for the disease to develop and were examined by the authors; pronounced spasticity of the lower limbs was observed in 3, and in the other 2 there was definite evidence in the lower extremities of pyramidal involvement. Signs of a pyramidal lesion were noted in the 2 children of one of the patients showing spasticity. Of 5 children born to one of the patients with changes in the reflexes only, similar signs were observed in 2 of the 3 who were examined. As additional constitutional features, note was made of the unusually firm and well developed musculature and a tendency to ichthyosis.

All 5 members in the seventh generation coming to the authors' attention appeared to be somewhat retarded mentally. Psychiatric examination of the 3 members who were in the advancing stage of the disease revealed, in addition, emotional instability and other evidence of organic dementia. Members of the family belonging to collateral lines not affected by the heredodegeneration, furthermore, occupied a generally higher social level. In their discussion of the genealogic implications, the authors expressed the view that the condition was a dominant hereditary trait.

DANIELS, Denver.

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